COLD INJURY

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Edited by
M. IRENE FERRER
ASSISTANT PROFESSOR OF CLINICAL MEDICINE
COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS
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ERRATUM

First Conference on Cold Injury

Page 232, line 9 For "twenty-two weeks, read "two weeks."

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PARTICIPANTS

Second Conference on Cold Injury

MEMBERS

JOHN H. TALBOTT *Chairman*
Department of Medicine, University of Buffalo School of Medicine
Buffalo, N. Y

M. IRENE FERRER, *Secretary*
Department of Medicine, Columbia University College of Physicians and Surgeons
New York, N Y

EDGAR V ALLEN
Division of Medicine, Mayo Foundation for Medical Education and Research,
University of Minnesota
Rochester Minn.

ALBERT R BEHNKE, *Captain* (MC) USN
Naval Radiological Defense Laboratory Hunters Point Naval Shipyard
San Francisco, Calif.

JOSEPH R. BLAIR, *Lt Col* (MC) USA
Department of Medical Military Science, Harvard Medical School
Boston, Mass.

GEORGE E. BURCH
Department of Medicine, Tulane University School of Medicine
New Orleans, La

ALAN C. BURTON
Department of Biophysics, University of Western Ontario Medical School
London, Ontario Canada

JEROME W CONN
Department of Internal Medicine, University of Michigan Medical School
Ann Arbor Mich.

JEFFERSON M. CRISMON
Department of Physiology Stanford University School of Medicine
Stanford, Calif

STEVEN M. HORVATH
Department of Physiology State University of Iowa College of Medicine
Iowa City Ia

ROBERT KARK
Department of Medicine, University of Illinois College of Medicine
Chicago, Ill.

HARRIS B SHUMACKER, JR.
Department of Surgery Indiana University Medical Center
Indianapolis, Ind.

PAUL A. SIPLE
Environmental Research Section, Research and Development Division
Department of the Army
Washington, D C.

JANET TRAVELL
Department of Pharmacology Cornell University Medical College
New York, N. Y

GUESTS

JACK ADAMS-RAY
Department of Surgery, Karolinska Institute
Stockholm, Sweden

KENNETH M. BRINKHOUS
Department of Pathology, University of North Carolina School of Medicine
Chapel Hill, N. C.

LOUIS-PAUL DUGAL
Department of Experimental Physiology, Laval University Medical School
Quebec, Canada

ALBERT H. HEGNAUER
Department of Physiology, Boston University School of Medicine
Boston, Mass.

H. T. MERYMAN, *Lt. (MC) USN*
Naval Medical Research Institute, National Naval Medical Center
Bethesda, Md.

KENNETH D. ORR, *Lt. Col. (MC) USA*
Army Medical Research Laboratory
Fort Knox, Ky.

LEONARD M. SCHUMAN, *Comdr. (PHS)*
Army Medical Research Laboratory
Fort Knox, Ky.

DONALD R. WEBSTER
Experimental Surgical Laboratories, McGill University
Montreal, Canada

The Josiah Macy, Jr. Foundation

FRANK FREMONT-SMITH, *Medical Director*

JANET FREED LYNCH, *Assistant for the Conference Program*

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THE JOSIAH MACY JR. FOUNDATION CONFERENCE PROGRAM

When I was on a destroyer out at Bikini in 1946 I was fascinated listening to our radio operator as he tested communication equipment. He would ask another ship through his radio, "How do you hear me?" and the answer often would come back, "I hear you Nine-Nine-Nine. That meant that everything was satisfactory Of the three nines one was for intensity one for clarity and one for meaning.

The Josiah Macy Jr Foundation has organized and devoted a large portion of its resources in support of its Conference Program because the officers are cognizant of the fact that there is obstruction to communication and mutual understanding across the disciplines and specialties, and that this, in fact, is one of the major factors delaying scientific advance. We feel that there are psychological factors, as well as semantic factors contributing to the difficulty of communication people even in arguments with one another are too much inclined to make statements *at* rather than to communicate *with* the others. I think that we are inclined to forget, though, that the real question is, are these words and statements those which are likely to convey to the listener the whole or even a small part of what I would like to express

I have a feeling that we should be very much concerned with the other fellow's receiving set and not only with our own transmitter If the other person doesn't seem to understand us, it may not be enough merely to increase the power of our transmission we must try to find the obstruction in his receiving set, and see what kind of filters and resistors he uses. So if we call out to the interprofessional no-man's-land, "How do you hear me?" and the reply comes back, "I hear you Nine-Nine-Nine, we have the beginning of communication. What we try to do in these conferences conducted by the Foundation is to set the stage for meaningful communication.

With the accelerating rate at which new knowledge is accumulating and with the increasing recognition that nature is of one piece, it becomes evident that the continued isolation of the several branches of science from one another is a serious obstacle to scientific progress. Nowhere in science is the need for combined opera-

tions more evident than in medicine. Today to be effective medical research and practice must embrace data from all the disciplines including nuclear physics at one end of the spectrum and cultural anthropology at the other for advances in one field are frequently dependent upon knowledge derived from quite another discipline.

Although fertility of the multidiscipline approach is thus recog nized, universities and scientific societies and journals which are usually restricted to one small area of a field in their coverage, have not yet made adequate provision for channels of interdisciplinary communication. We do not wish to compete with the formal scientific meetings or with the scientific journals which have established patterns and formats for the presentation of material. Our purpose at the meetings is to keep an informal atmosphere and to encourage the exchange of methods research plans, concepts and difficulties, which cannot be done if there is formal speech making.

The Foundation has endeavored to meet the need for inter disciplinary communication by bringing together for a series of two-and-a-half day annual conferences a small group of investigators, representing in so far as possible all the branches of science which bear on a chosen problem. Participants in these informal conferences over a five-year period develop a feeling of friendship trust and mutual respect which in turn promotes communication, cross-fertilization of ideas and cooperation. The success of such an endeavor however is dependent upon full participation of all members in the discussion. Accordingly attendance at any conference is limited to twenty five.

Under the guidance of Dr Willard C. Rappleye, President of the Foundation since 1942, the Conference Program has been gradually expanded and enlarged until during 1953 it included twelve different groups, meeting annually to discuss a wide variety of problems in the field of medicine and the closely related disciplines. Our plan is to discontinue the meetings of each group at the end of five years.

In order to share with a wider group of investigators and students the essential quality of these conferences and to give others an insight into the functions of the scientific mind, the informal nature and tempo of the discussions in so far as possible are preserved in the published transactions.

FRANK FREMONT SMITH, M.D
Medical Director

INTRODUCTORY REMARKS

JOHN H TALBOTT
Chairman

For this conference, we attempted to select members, as well as guests, who were interested in fundamental research upon cold or who were interested in the investigation of the basic problems in so far as the physiological and the pathological effects of cold are concerned. But there are two very obvious practical implications that are unavoidable. To gather more information regarding the causative mechanisms of frostbite is one important clinical problem in the field. Although progress has been made, frostbite remains as an injury without a readily available form of therapy So long as there are military operations in cold countries, and there are going to be more, I think, rather than less in the years ahead, frostbite and cold injury will still be an important problem for the armed forces. The other clinical problem is hypothermia which received some civilian clinical impetus 15 or 18 years ago, but the interest waned considerably during the war years. During the past two or three years, it has been revived, particularly as a tool in the handling of certain surgical problems, and even though hypothermia is not one of the scheduled, formal subjects for discussion, we certainly want to spend some time in bringing ourselves up to date on the various aspects of hypothermia that are of direct clinical interest to most of us

At our first conference, we said nothing about the epidemiology of frostbite. I wasn t sure that such a subject was amenable to study However an epidemiologist was included in the second frost bite team to Japan and Korea, and I think that the results which Dr Schuman was able to bring back amply justified the assignment of such an investigator Epidemiology of frostbite was, to me, a very enlightening and a very stimulating aspect of the whole cold problem, and that was the reason why we chose it to be the first topic discussed at our second conference.

EPIDEMIOLOGY OF COLD INJURY IN MAN

LEONARD M SCHUMAN Comdr PHS*
Army Medical Research Laboratory
Fort Knox Kentucky

EPIDEMIOLOGY as I define it, is merely a study of mass phenomena of disease or trauma. With that simplified and shortened definition I believe we can understand each other very readily The epidemiologic approach to cold injury was a rather intriguing one to me because it represented a chance to apply certain epidemiologic principles which had been explored in great detail during World War II by John Gordon of Harvard and by Colonel T F Whayne, of the U S Army Frostbite, as you undoubtedly have recognized from the very beginning of your own personal studies, is of multiple causation and has multiple modifying factors, and so it was felt that the epidemiological approach was the only approach that could easily elicit certain relationships between the host, his environment, and the particular agent, namely cold, and its synergist, wetness.

The epidemiologic approach, has within itself certain difficulties, just as has any other regimen of science. For example, direct measurement of certain factors is not always possible, because frequently we are dealing with attributes rather than with measureable quantities.

Kark: You mean the attributes of the person who is injured?

Schuman: Yes, the attributes on the part of the person injured, as well as the attributes in the so-called socio-economic environment, e.g. morale, training, and orientation. In the past the role of a given factor has been studied more or less by comparison between two groups, and in this way the epidemiologic approach has yielded results. It also presents certain difficulties because in the field one cannot always control the attributes with which we are dealing On the other hand, we don t always want to control those attributes because we will be disturbing the natural relationship between the host and the agent. Frequently a given factor may seem physiologically rational and yet not prove to be so in an actual analysis

*Presently Deputy Director Illinois Department of Public Health, Springfield, Illinois

of the data collected. As an example, I would like to interject here our experience in analyzing the significance of the smoking done by the soldiers which in a sense, is a measurable variable. We found the very reverse of what we expected to be true. The controls which we obtained in this particular study actually smoked a significantly greater amount of cigarettes than did the patients.

There were quite a number of problems that remained unsolved at the end of World War II first of all, the role of cold as the agent determining the gradient of injury in other words, can we set up certain criteria of temperature at which point or points a certain degree of injury would take place? I believe that before this presentation is over we will have presented some clues to the establishment of such a gradient.

Second, is it possible to predict accurately the incidence of cold injury from the anticipated temperatures in the field?

A third problem was the relation of duration of exposure to temperature, which is also intimately tied up with the idea of a gradient of injury There was the problem of the synergistic effect of wetness, that Colonel Whayne and his team (1) presented in an excellent monograph but here, too, no one has thus far attempted an analysis of this factor to determine its significance in cold injury

There are other less easily measured factors or variables namely training of the individual, which involves not only the teaching of combat techniques and general education but also a development of the soldier s motivation and his indoctrination to military tactics; the phenomenon of fatigue, which has been defined as being proportional to the product of intensity and duration of stress, although we do not have good measurable indices for the role of fatigue in the production of cold injury nutrition, which to me has always represented a field in which there is a great volume of endeavor and literature, but which still lacks quantitative studies applicable to man with respect to its role in cold injury There are still other factors that remain unanswered today These include the social factors in combat fatigue; the relationship of incidence of neuropsychiatric disorders to cold injury the role of intelligence, for although intelligence is reasonably measurable, still we have not satisfied ourselves as to the relationship between the intelligence of the individual or the group and the incidence of cold injury Morale is another factor that is difficult to assess. We have tried in this connection to measure differences of morale among various units of organization in the Eighth Army especially when certain previous writers have indicated that the venereal disease rates, the accident

rates, and the incidence of disciplinary measures brought to bear on certain combat units are measures of the morale of the group in other words, these rates are low in a group with high morale. We felt, too, that because cold injury was in a sense an accident of exposure, possibly there would be a relationship between the morale of the unit as manifested by the over-all accident rates or nonbattle casualties and the actual cold injury rates.

Motivation, which is another factor that has been described and which Colonel Whayne has attempted to assess in his monograph, is also a variable which is rather difficult to measure. It involves the use of reward for achievement, and tactical and strategic orientation of troops within the limits of security But how can we measure the level of such motivation?

Then, another large group includes the factors within the socio-economic environment of the soldier himself We have long recog nized the fact that cold injury is a definite occupational disease of the frontline rifleman, and I have material to indicate that even on a static defense front, such as we had in Korea in the winter of 1951-52, this phenomenon still holds true. Combat activity can be measured a little bit better but it is not a sole determinant. Not only does combat activity modify the incidence of cold injury but is itself in turn modified by other factors. One must mention the availability of shelter and clothing, which can be properly measured. Command leadership and attitude, however are other difficult-to-measure factors. Good hygiene and discipline which go into the broad picture can be measured, but not as well as some of the other factors.

In our experience in Korea, we definitely applied the so-called survey approach. We can not readily alter field conditions to control certain factors, while still other factors are permitted to vary so that we can get the measurement of the range of variability and its effect upon cold injury The survey approach therefore is deemed the most likely and the most natural one for an analysis of the various factors that enter into the production of cold injury because it is one which takes place prior to is continuous with, and follows the incidents themselves. This type of approach, proved in many instances in communicable disease, will preserve the normal rela tionships and the true perspective of the variables which are involved.

In the winter of 1951-52, there were three aspects to the surveys performed first, the interviewing by predetermined standards, techniques and question content, of a patient who was injured,

second, the interviewing of a group of controls, whom I prefer to call bunker mate controls, for they were in the identical environmental location as the cold injury patient himself In other words, our sampling was deliberately not random. We wanted one thing in common, that the controls should have been exposed to the same environment as the patient with cold injury

Horvath Was this second group hospitalized also?

Schuman The second group was not hospitalized at all. This was a group of front line soldiers who were on the same combat patrol with the patient with cold injury on the same night or the same day

Horvath And the interview was conducted in what relationship?

Schuman The interviews of the controls were conducted in the same fashion as they were in the case of the patient. The questions asked of the patient when he arrived at the hospital were also asked of the controls when visited by the interviewer in their front line position.

Horvath Well, I was wondering within what time interval, a week or a day or what?

Schuman An attempt was made to obtain the answers to these questions within a week or two. In some instances, as much as three weeks elapsed between the onset of cold injury in the patient and the interview with the bunker mate.

Kark The interviews were conducted forward?

Schuman They were forward. For the most part the control came back to, say the forward battalion aid station, and on occasion he was interviewed in mortar positions on reverse slopes of front line hills. We saw a good deal of the front lines that way We tried to get these controls as soon as possible after the cold injury in the patient by finding out the exact unit from which the patient came, discussing the situation with the battalion commander to find out what activity this patient was engaged in, and then hunting for the control who was with the patient at the same time on the same night. Fortunately these commanders keep a log of all their daily activities and could pinpoint the exact time. The amazing thing is that the controls whom we interviewed gave highly reliable information as confirmed by checking with commanders and medics. If we questioned them closely as to what time of the day or night the action occurred, it corresponded well with the commander s log of that particular activity We could not at first believe that we could obtain such good recall from this group, but I attribute the success of the interview to the static front at the

time, the relatively short time interval between the incident and the interview and the rapport established during the interview

Webster Was the interview privileged, so that the control wouldn t fear any disciplinary reaction?

Schuman Oh, absolutely It was kept confidential and done privately without even the medical officers present. They assisted only in getting the controls into the battalion aid stations. We set the criteria for obtaining these people rather than the medical officers. In the interviews a purely medical and epidemiological history was taken. A psychiatric phase was done later in another section of the study

Horvath Have those questions that you set up been analyzed since that time on the basis of being weighted in one direction or another or did you not have a formal pattern of questions that you asked?

Schuman: These questions were not analyzed as to weighting, because of the nature of the questions, which included such queries as the hour of injury what were they wearing at the time of injury the kind of footgear the kind of sock, what state they came from, their race, how many hours before they went out on this patrol did they have their last meal, and what did the meal consist of – in other words, such vital data as are pertinent to any medical questionnaire. These were not questions necessarily designed to obtain psychological attitudes or responses.

Horvath Who did all the questioning? One individual?

Schuman: Yes, I did all the questioning of these controls. As far as coterminality in space and time goes, if a man went out on a combat patrol, then a man who was in the identical squad with him was selected for the control interview He had to be in the same place at the same time and engage in about the same type of activity If he were in a tank and were a gunner we would select one of two types of controls: another gunner in a tank alongside of him, or the ammunition handler within the same tank as the patient. If the patient were riding a vehicle and was frostbitten, then the man who was on the same truck with him was selected for the interview if the patient stood guard, and if it were a two-man guard, of course, the man who was on guard at the same time was questioned. If it were a one man guard we took the man who preceded the patient or succeeded him on guard duty in that same spot on that particular night. And so it went. We set the conditions, and in that respect, the sampling was not random. There was one peculiar characteristic of the sample which will be pertinent to

what you will see in some of the figures, namely that the number of controls among Negroes was very very low That can be explained by the fact that about nine or ten per cent of the population of a unit was Negro. Thus in a squad of eight or nine people if you had one Negro and he was frostbitten, you wouldn't have any more Negroes from whom to select your control sample. Rather than just take Negroes in any other squad, which we felt would be defeating our purpose of coterminality in time and space in that particular exposure we took a white man instead, and we have other means of analyzing these differences.

In a third aspect of the survey I was able to utilize a great deal of the data even though the initial purpose of this pre-exposure survey was not fulfilled. This phase was performed to establish certain baselines on subsequent cases of cold injury that would develop during the year Unfortunately with the amount of personnel involved, we were able to obtain only 1600 interviews, and found only two subsequent cases of cold injury among those. However the data collected in that study served as a good cross section sample of the front as a whole.

I believe that the reliability of the data which we collected was of high order as evidenced by the fact that the stories we were able to get out of the controls coincided very well with the stories that were obtained from the patients after they were hospitalized. This, of course, was further checked with the stories that the battalion commanders had to tell about a given operation just what was happening at the time, the intensity of action, how badly they were pinned down, how much movement they could perform, etc., in a particular situation.

In 1950-51 a good start had been made on the collection of data for a mathematical evaluation of the factors that I have mentioned. By the next year however it was evident that the two experiences, namely the 1950-51 experience and the 1951-52 experience, differed markedly in the type of action that was engaged in. In 1950-51 the investigators had a chance to measure the interplay of combat activity because at that time we were involved in both a retrograde movement, in which there was a high casualty rate and an active-defense type of strategy In 1951-52, the type of activity changed to one of static defense, so that combat activity as a variable could be considered as controlled. Such a static front, of course, permitted the measurement of certain variables which could not be measured the winter before because of the rapid flow of troops across the area in fact, an epidemiologist would not have been

tolerated in 1950-51 as he was in 1951-52 when we were able to get into front line bunkers in some instances.

In 1951-52, the incidence of cold injury fell dramatically mainly because we had lessened activity a better supply of gear and the rubber insulated boot. We had a rate of 3 per 1000 per annum confirmed cases of frostbite across the entire front. November had the highest incidence. In December the rates fell, and in January and February the rates increased again, and by March they tapered off to virtually zero.

Kark Will you define "frostbite, please? You said 716 cases of frostbite.

Orr Frostbite is an injury that occurs as a result of exposure to a low ambient temperature (less than 25° F) over a relatively short period of time (less than 72 hours but usually 4 to 8 hours) The injury is classified into four degrees of severity The injury among combat soldiers is usually localized to the foot or hand.

Kark You would call a frostbitten ear a frostbite?

Orr: Yes, if a logical history and certain symptoms are elicited. In order to be considered frostbitten the patient should be able to relate events of his cold exposure, rewarming and symptoms such as burning stinging pains and paresthesia. Pertinent signs of injury such as, edema, hyperemia, vesiculation or desquamation should have been noted. It should have been severe enough for him to go to the medic.

Blair You might also say that frostbite is an injury that could not occur at ambient temperatures above 25 F Any injury occurring above that ambient temperature could not be frostbite.

Orr: That s right.

Burch Are any of these trench foot?

Orr I have not seen trench foot in Korea during the past two winters. The cases we had in Korea were not similar to those seen in Italy during the winter months of 1944-45.

Schuman. Table I shows that cold injury remained an occupational disease of the front-line rifleman. You will note the attack rate for the Eighth Army as a whole was 3.04 per 1000 per annum. The divisional rate was 5.95· the regimental rate was 8.78 and the battalion rate was 11.79 These represented the following percentages of all the frostbite cases in the Eighth Army 92 per cent of the cases were in divisions, 81 per cent were in regiments, and "6 per cent in battalions. These particular echelons, on the other hand represented the following strengths in the Army as a whole namely divisions, 47 per cent of the Army regiments, 28 per cent

TABLE I

Comparison of Total Frostbite Attack Rates for the Several Echelons in the U. S. 8th Army Korea 1951-52

Unit	Attack Rate/1000	( ) % of 8th Army Cases	(b) % Strength in Army	(a/b) Ratio of Actual Rates to Expected Rates	(c) % of Division Cases	(d) % Strength in Divisions	(c/d) Ratio of Actual Rates to Expected Rates	( ) % of Regt. Cases	(f) % Strength in Regt.	(e/f) Ratio of Actual Rates to Expected Rates
8th Army	8.04	100.0	100.0	1.00	—	—	—	—	—	—
Divisions	5.95	92.2	47.2	1.96	100.0	100.0	1.00	—	—	—
Regiments	8.78	81.2	28.1	2.85	88.1	59.7	1.48	100.0	100.0	1.00
Battalions	11.79	76.4	19.7	3.88	82.8	41.8	1.98	94.1	70.1	1.34

Infantry battalions only (rifle and mortar companies)

of the Army and battalions approximately 20 per cent of the Army as a whole.

When we calculate the ratio of actual attack rates to the expected rates, the latter representing the values expected if the rate of cold injury had been uniform irrespective of echelon or unit, we find rather interesting mathematical ratios. At the division level, the rate was almost twice that for the Army as a whole the regimental band, represented the following strengths in the Army as a whole and the battalions had a ratio approximately four times that for the Army as a whole, indicating that when we get to the battalion level the rate of cold injury is four times that which would be encountered in the Army as a whole, including all the elements of rear troops service units etc. Now if we make the same calculation taking the division as the base-line, we find the following ratios to hold 1, 1.5 and 2 for division, regiment and battalion, respectively If we use the regiment as the base-line, we find that the battalion has approximately half again as many cases as would be expected with a uniform attack rate for both units, that is if the occupational character of this particular injury were disregarded. Thus, in Korea in the past year cold injury remained a disease of the front line rifleman.

Burton Would you relieve my ignorance, coming from a foreign country so to speak? To me, a Canadian, the terms division regiment "battalion would really be categories of size of units With you, they evidently are not. Is the battalion a group of men who do different things from people in a regiment?

Schuman The battalion can be thought of as that unit which has the greatest concentration of actual front-line riflemen The regiment has three such battalions, plus certain other service battalions, and all the ancillary support troops. Similarly the division has the three regiments that we mentioned, plus additional support troops just as the army itself has three or more divisions with all its support troops.

The number of support troops up to and including the regimental level, on the average, is roughly equal to the number of active fighting men. This can be seen in Table I at the division level where you find 47 per cent of all the troops in the Eighth Army are represented in all the divisions, the difference being the support troops for all those divisions. The same differentiation would apply to the regiments. All the regiments that were present in Korea at that time represent 28 per cent of the entire strength of the Army The difference 72 per cent, was all support troops In the same

way the battalions represent 20 per cent of all the Army and 80 per cent are support troops.

Meryman Are all the battalions that you refer to here infantry battalions or do they include others?

Schuman No, only infantry battalions, but they represent all the infantry battalions that were deployed across the lines in Korea. Support battalions like tank, engineer signal and so on, are not included as infantry battalions These are regimental or divisional support. Only the infantry battalions which contain the rifle and heavy weapons companies are included here.

Horvath Is there any relationship that you found between the relative number of cases in the battalion *per se*? The interesting point it would seem to me, is how many of those support troops of the battalion were afflicted with frostbite and how many of the actual individuals engaged on the static front were afflicted.

Schuman That is not shown in the table, but it can be derived by a simple calculation. If you will take the difference between the number of cases in the battalions and in the regiments and divide by the difference between the total battalion strength and regiment strength, you will then have the rate for regimental support units. It is well to point out that these battalions on whom the calculations in Table I were made represent 100 per cent front line rifle and heavy weapons companies. They are the three combat battalions in each regiment, including mortar companies which are engaged in active combat. The supporting elements of the battalion were tallied as part of the regiment to which they belong. A few support troops within the battalion, those attached to the headquarters group the medical men or the corpsmen who actually go out on combat patrols, were considered part of the combat battalion if they themselves were injured. Also intelligence and reconnaissance groups from headquarters were considered front line elements because they were stationed on the main line of resistance and engaged in missions in no-man s land.

Burton *I think this particular use of words in your report* might lead to some misunderstanding, particularly abroad.

Schuman I am glad to have it brought to my attention. If there is that confusion, that will have to be corrected to read "combat battalions only or some such designation. Would that clarify the picture?

Meryman Is that also going to apply to regiments? Are those combatant regiments?

Schuman No, the regiment includes the three combat battalions

and all their supporting units. Other units which might total regimental strength are not designated as regiments within the division. There was a tank battalion supporting or attached to a regiment but that was still considered a divisional unit rather than a part of the regiment.

Burch Do you have an analysis of your data which shows the distinction between the men who do have an opportunity to warm themselves such as the medical corpsmen who may go in and out of battalion aid stations and warm their hands and feet, and combat soldiers who do not?

Schuman We have that data only in a general way. Our Quartermaster observer made a study in which he showed what percentage of the patients did have the opportunity for warm-up and which did not. Unfortunately, we do not have a standard of reference to the number of troops, who had shelter available at the time. May I add that medical corpsmen go along on combat patrols as well and are not necessarily in and out of battalion aid stations.

Shumacker Could we assume that the attack rate would correlate quite closely with the hours of potential exposure to severe cold per man? In other words, the number of hours of exposure of the Eighth Army personnel as a whole would be small because a great many men were not exposed to severe cold. When you get down to the battalion level, however, the percentage would be much higher. For that reason this seems very significant.

Schuman Right, that is exactly why I say that cold injury is an occupational disease of the front-line rifleman, because of this element of exposure. I would say that this is not because it may represent one-fourth of the men exposed to cold, because the number of men in the battalions is actually 20 per cent or one-fifth of the entire strength of the Eighth Army, yet 76 per cent of the total Eighth Army cases are found in battalions, virtually four times the attack rate that you have for the Army as a whole. To separate out the purely supportive elements, you would have to recalculate the rate by using the difference between purely battalion cases and total cases divided by the difference in strength between the total of battalions and the Eighth Army as a whole. Such a calculation leads to an attack rate of 0.92 per thousand for all support troops as compared to 11.8 for battalions, that is, the attack rate for battalions *per se* is now 12.8 times that for support troops, rather than four times the value for the Eighth Army as a whole.

As to the reliability of the data which we gathered, I would like to emphasize that we were not satisfied with merely the patient's

way the battalions represent 20 per cent of all the Army and 80 per cent are support troops.

Meryman Are all the battalions that you refer to here infantry battalions or do they include others?

Schuman No only infantry battalions, but they represent all the infantry battalions that were deployed across the lines in Korea. Support battalions like tank, engineer signal and so on are not included as infantry battalions These are regimental or divisional support. Only the infantry battalions which contain the rifle and heavy weapons companies are included here.

Horvath Is there any relationship that you found between the relative number of cases in the battalion *per se*? The interesting point it would seem to me is how many of those support troops of the battalion were afflicted with frostbite and how many of the actual individuals engaged on the static front were afflicted.

Schuman That is not shown in the table, but it can be derived by a simple calculation. If you will take the difference between the number of cases in the battalions and in the regiments and divide by the difference between the total battalion strength and regiment strength, you will then have the rate for regimental support units. It is well to point out that these battalions on whom the calculations in Table I were made represent 100 per cent front line rifle and heavy weapons companies They are the three combat battalions in each regiment, including mortar companies, which are engaged in active combat. The supporting elements of the battalion were tallied as part of the regiment to which they belong. A few support troops within the battalion, those attached to the headquarters group the medical men or the corpsmen who actually go out on combat patrols, were considered part of the combat battalion if they themselves were injured. Also intelligence and reconnaissance groups from headquarters were considered front line elements because they were stationed on the main line of resistance and engaged in missions in no-man s-land.

Burton I think this particular use of words in your report might lead to some misunderstanding, particularly abroad.

Schuman I am glad to have it brought to my attention. If there is that confusion, that will have to be corrected to read combat battalions only or some such designation. Would that clarify the picture?

Meryman Is that also going to apply to regiments? Are those combatant regiments?

Schuman No, the regiment includes the three combat battalions

and all their supporting units. Other units which might total regimental strength are not designated as regiments within the division. There was a tank battalion supporting or attached to a regiment but that was still considered a divisional unit rather than a part of the regiment.

Burch Do you have an analysis of your data which shows the distinction between the men who do have an opportunity to warm themselves, such as the medical corpsmen who may go in and out of battalion aid stations and warm their hands and feet, and combat soldiers who do not?

Schuman We have that data only in a general way Our Quartermaster observer made a study in which he showed what percentage of the patients did have the opportunity for warm-up and which did not. Unfortunately we do not have a standard of reference to the number of troops, who had shelter available at the time. May I add that medical corpsmen go along on combat patrols as well and are not necessarily in and out of battalion aid stations.

Shumacker Could we assume that the attack rate would correlate quite closely with the hours of potential exposure to severe cold per man? In other words, the number of hours of exposure of the Eighth Army personnel as a whole would be small because a great many men were not exposed to severe cold. When you get down to the battalion level, however the percentage would be much higher For that reason this seems very significant.

Schuman Right, that is exactly why I say that cold injury is an occupational disease of the front line rifleman, because of this element of exposure. I would say that this is not because it may represent one-fourth of the men exposed to cold, because the number of men in the battalions is actually 20 per cent or one-fifth of the entire strength of the Eighth Army yet 78 per cent of the total Eighth Army cases are found in battalions, virtually four times the attack rate that you have for the Army as a whole. To separate out the purely supportive elements, you would have to recalculate the rate by using the difference between purely battalion cases and total cases divided by the difference in strength between the total of battalions and the Eighth Army as a whole. Such a calculation leads to an attack rate of 0.92 per thousand for all support troops as compared to 11.8 for battalions, that is, the attack rate for battalions per se is now 12.8 times that for support troops, rather than four times the value for the Eighth Army as a whole.

As to the reliability of the data which we gathered, I would like to emphasize that we were not satisfied with merely the patient's

response to questioning. In our initial hunt for the particular bunker mate control, we interviewed the battalion commanders to find out the exact situation in which this particular patient had been frostbitten and from that information, we were then able to ask questions of the bunker-mate control, which would prompt his recalling the situation. It has been mentioned that this type of questioning is always difficult at best. I would like to say that I personally interviewed these people and, on the basis of all my past experience in conducting this kind of survey inquiry I feel that we established very fine rapport with all the controls who were interviewed. I feel that these boys were answering to the best of their ability at the time, that they were not giving fictitious answers, because there was no element of recrimination involved. These boys were prodded into giving us the true situation at the time by telling them a little bit about the situation that we were trying to get them to recall. Fortunately there were many incidents which would remind the boy of the situation at the time and bring forth quite a bit of information that we were seeking. There was, however a type of data that was not reliable- for example, "How much weight did you lose?" I think these latter answers reflected certain elements of immaturity in the individual and what he felt about his own person rather than an exact estimate of weight change.

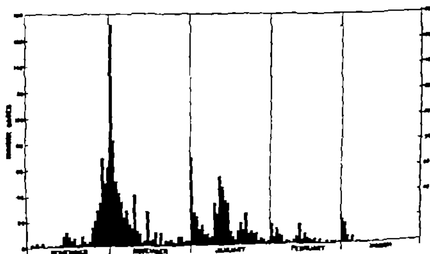


FIGURE 1. The dates of occurrence of frostbite during the winter of 1950-51 in 1710 cases subsequently hospitalized at the Osaka Army Hospital. Reprinted, by permission, from Orr, K. D., and Fainer D. Cold injuries in Korea during winter of 1950-51. *Medicine* 31: 177 (1952).

Figure 1 represents a sample of the situation in the 1950-51 winter This figure is presented so that the identity of the pattern can be seen between it and the pattern in 1951 52 shown in Figure 2. At the beginning of the 1950-51 winter season, there was a sharp increase in cases, almost epidemic in form, then a decline through the month of December and then peaks in January lessening in intensity through February and tapering off in March.

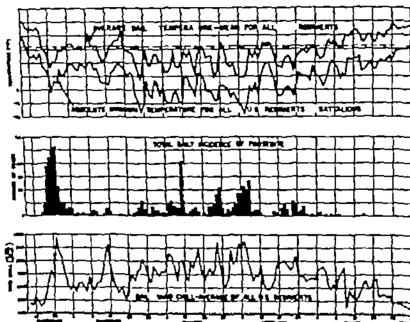


FIGURE 2. Daily incidence of frostbite and selected weather data for the U.S.-Korean Front for 1951-52.

Figure 2 shows that we had an epidemic type of curve at the beginning of the 1951-52 season, about the same time as the previous year despite the difference in the over-all intensity of combat activity However there was an element of similarity even there for we were hit by the enemy along the line in two or three spots at a time of an interchange of position between our regiments and the ROK troops The United States regiments in question were caught without their shoepacs. They were on hills, desperately digging into positions that were too shallow for them as they had

been occupied previously by ROK troops of shorter stature, and the first cold wave hit at the same time. It was as if the enemy utilized the cold spell as well as the interchange of positions to attack us. That was the only flurry of combat activity in the entire winter of 1951-52 that could even compare to the type of activity that existed in 1950-51, with its retrograde action and its very active defense which finally turned into offensive action but not without units being pinned down in many situations.

Burch Was any attempt made by our army to change troops during warmer weather and to avoid making changes during cold spells that are known to be approaching the battle area?

Orr I do not believe so. At least not until after November 1951. One of our objectives in the cold injury program in 1951-52 was the indoctrination of combat troops in the application of weather data and the prediction of weather changes. This approach allowed smaller units to take into account the weather whenever they made changes in position, sent out patrols, etc.

Burch Is that a practice to be instituted or one which has been in practice for some time?

Schuman That is a practice to be instituted, for the most part. Some of this was begun in one or two regiments before we left, on the basis of their very favorable interest in weather and its application to tactical situations, operation of equipment, and so on.

Siple Yes, the local regimental and battalion weather observation system started by the Cold Injury Team has been preserved and improved.

Shumacker I imagine, George, that Commander Schuman will bring out later the fact that up until the winter of 1951-52 the Army had no apparatus or trained personnel for actually measuring or predicting weather conditions on the fighting line. It was a part of the study team's program to institute such studies. It met with such general approval and its usefulness was so apparent that it has now become a permanent part of troop operations.

Burch You mean there had been no weather prediction on the front lines? That is a very practical military problem!

Schuman Right, and it is pertinent to the ensuing discussion here. After all, there is a basis for all the temperature curves that you see in Figure 2. Prior to the experience in 1951-52, the only temperature data that were available were either from division air strips or the Air Force stations themselves. These were frequently miles and miles from the front lines, many times 20 or 30 miles south of the front lines. In 1950-51 the nearest airport in use was

more than 100 miles south of the Chosen reservoir There was no way of getting local data at the time. Therefore at the beginning of this study one important consideration was to obtain weather data as close to the locale of injury as possible, and I think that for the first time in the history of military operations we got as close as anybody could get, to the battalion command post, which frequently was right on the ridge near the bunkers with the front-line elements of the troops

Burch I think it is rather interesting that the local weather has not been exploited to its utmost in ground operations.

Siple I can explain the situation in part. Coincidental to the program of military department unification, an effort was made to cut down services. In consequence the Army by agreement receives its weather information from the Air Force. This reliance on the Air Force has become so deep-seated that all the meteorological training, thinking and planning has been greatly reduced within the Army However the Air Force has not actually entered into the problems of the Army to ferret out the Army's needs, nor has the Army maintained personnel in the meteorological areas who were trained and technically able to request the kind of service it needs. This situation has existed since World War II, when the agreement was first made. The inefficiency which resulted is recognized and steps are being taken at present to effect improvements. Of course, they have had formal weather forecasts. However the forecasts that Commander Schuman is referring to were issued out of Seoul. From the beginning of the Korean war there has been a central Air Force weather station from which daily forecasts are issued. When these are applied to local positions 50 or 100 miles away from the actual site there are significant variations.

Shumacker It certainly seems a great advance now to have weather measurement and forecasting as a standard part of troop operations.

Adams-Ray Is there something here in the rapid changes of temperature that gives more cases of frostbite? Not only the going down but also the going up of the temperature? If you have a sustained period of very low temperature, you do not have many cases of frostbite but with rapid fluctuations in temperature you seem to have higher incidence.

Schuman Well, I have not personally observed that kind of phenomena. There is a pretty good correlation between the actual daily incidence and temperatures in Figure 2. As previously mentioned the experience in the winter of 1950-51 led to the establish-

Siple It wasn't poor selection of clothing which caused that, then?

Schuman No The peak more or less reflects the temperature drops again. The statement has been made that the best correlations would be with wind chill. Actually correlations are just as good with average temperature as with daily minimum temperatures. I was ready to accept wind chill as the best correlative factor until the particular data presented themselves, but I think it must be said that the terrain of Korea operates against wind chill being a highly correlated factor because, whereas, a wind may blow down a valley a mountain may block off that wind fairly well for a particular line, and so you get under these conditions a detracting effect upon the correlation with wind chill.

I feel that the large peak in November is predominantly a result of *a*) the most intensive combat activity of the whole experience, and *b*) *the failure of the troops to don the right kind of gear* at the time. Those are overshadowing factors. We have no evidence for lack of acclimatization other than that the large incidence occurred with the first cold wave. I really cannot say that that phenomenon exists except philosophically and as far as experience is concerned, we do not have data to back it up It could be a factor in this particular first major peak.

Kark Is this not also a phenomenon like immunity? Is this a population who have never been exposed to cold before and do not know how to look after themselves? In other words, there must have been some rotation from troops of the year before, with new fresh troops coming in who had never been in the cold. Do you have any data on that?

Schuman We know that rotation virtually removed from the theater the vast majority of those people who had had experience in the previous winter I can say that the number with a history of previous winter combat in the same theater was relatively small, and this includes both patients and bunker mate controls, so that lack of experience in winter fighting certainly cannot be ruled out.

Blair Another possibility is the elimination of highly susceptible individuals. We know that certain individuals with labile peripheral vascular systems, particularly hyperhidrotic persons, are especially susceptible to cold injury and that usually the first cold stress will eliminate these highly susceptible individuals and leave a much more resistant general population.

Schuman That is certainly a field that remains to be explored. We attempted the measurement of the vasomotor stability or

lability in the pre-exposure study by a test which Dr Burch (2) has described. Commander Cook, who was responsible for the pre-exposure studies, applied this test to 1,600 soldiers. These data unfortunately are highly unreliable because of the extreme variability of the environment in which the test was done. It had to be done in forward battalion aid stations, and sometimes they were well heated and crowded, so that the heat was excessive, and at other times the stoves would be out, and the light would be poor for the Coleman lanterns would be burned out. It is certainly worthy of further exploration to see whether or not susceptible persons are removed *en masse* with the first wave of cold.

Blair: It might be well to note that the cold injury pattern in Korea during the past two winters follows closely the pattern that occurred in Italy and in the Aleutians during World War II. There in each case, with the first onset of severe cold there was a tremendously high incidence of cold injury and although colder weather followed in January and February there was a lesser degree of cold injury Of course, this must be correlated with combat activity before it can be evaluated, but it appears to me that there must be factors of elimination of susceptible individuals, acclimatization, cold weather equipment, learning and discipline, to be considered in the over all picture.

Crismon: Two words came up in the previous discussion that I think are of considerable interest and concern the whole aspect of acclimatization. One of them is experience, which has both learning and exposure connotations, and the other is the more restrictive term, acclimatization. Did your data have anything in them which would permit you to distinguish between the learning aspects and the acclimatization aspects of this total exposure?

Schuman: I believe that our data demonstrate the operation of possible acclimatization prior to this exposure as a factor in this exposure rather than the factor of experience. Table II shows that no difference existed between patients and controls with respect to days in combat before frostbite. Although the bulk of patients were in combat for a short period of time when frostbite occurred, this was also true of the bunker mate controls. Thus experience in combat does not appear to have been a significant factor influencing frostbite incidence in 1951-52. As to acclimatization during this first phase of exposure of course, we can say little The bulk of the evidence seems to be in favor of prior acclimatization rather than experience in this particular situation.

TABLE II

Comparison of 679 Cases of Frostbite and 453 Controls with Respect to Days in Combat, Korea 1951-52

Days in Combat	Cases		Controls	
	No.	%	No.	%
0 – 15	192	28.3	113	24.9
16 – 30	125	18.4	84	18.5
31 – 45	65	9.6	59	13 0
46 – 60	51	7.5	32	7.1
61 – 75	35	5.2	19	4.2
76 – 90	39	5.7	27	6.0
91 – 105	32	4.7	21	4.6
106 – 120	34	5 0	37	8.2
More than 120	106	15.6	61	13.5
Total	679	100 0	453	100.0
X^2=9 9406 df=8 P>.20				

Burch Would you say that the instructions given to new troops concerning protection of themselves were adequate?

Schuman I don t think there is enough indoctrination or cold weather training You see marked differences in units and the pre-exposure studies showed a wide range in the amount of instruction that the troops received. There is always a little tendency on the part of a patient to make excuses for his injury when he thinks that there might be danger of recrimination, either by way of an accusation of self inflicted wound or that he wasn t very careful and that is why he was injured. There is a certain amount of bias that creeps into that kind of data however pre-exposure controls with no recriminations at stake present more reliable data, and on this basis I say that instruction indoctrination and actual cold weather training are inadequate.

Talbott I think that in addition to indoctrination, one must have experience Indoctrination is fine but the best indoctrination is going to fall far short of the ideal unless experience is superimposed.

Shumacker: Commander Schuman, Dr Adams-Ray raised a question about injuries sustained with rising temperatures from freezing levels. It has certainly been the experience of our armies in past wars and of all armies as far as I know that such periods are fraught with great danger of mass cold injuries. Baron Larrey of course pointed out this fact very dramatically in his account of the Napoleonic retreat. Don't you think the reason why there were no injuries sustained during exposure to weather above freezing in the Korean campaign is evident in the terrain and tactical situation? It was not necessary to keep men immobilized for days and weeks in wet trenches as it was in Europe during World War II. The conditions necessary for production of what we speak of as trench foot didn't exist. If a man could escape frostbite during periods of intense cold, he got by without cold injury

Schuman If Dr Adams-Ray is referring to that kind of situation, then you have given the answer I was thinking strictly in terms of frostbite when I said cold injury and I should be careful of that distinction. In World War II in Whayne's very painstaking description of the problem, that was a common phenomenon. It was when the ground thawed out and exposure to wetness for a long period of time occurred that a great incidence of trench foot was noted, and that was coincident with the rising temperatures of thaw

Webster Commander Schuman, have you any comparative data between the United States and the other United Nations units that were engaged there?

Schuman Yes, we have some. The best correlations that could be made were with the British troops. Their incidence rate was very low but we were unable to get their measure of combat activity in actual figures as measured by actual casualty rates They could have been obtained, and I am sure we will do it before the study is completed. However we think that their low rate was due to the type of activity in which they were engaged rather than, as they claim, the kind of boot they wear I can't accept that from observation and many others won't I am told that they would keep no-man's-land covered with artillery fire during the night and not send out any patrols and come off the positions which they occupied during the day Automatically the intensity of exposure was lessened thereby They would come back into warm bunkers, and go back the next morning. It was the type of warfare conducted, and the type of terrain they occupied on the western front in Korea, that made the difference I believe Whayne found that correlation

to be true in World War II. In addition, the British Commonwealth sector was, on the average, somewhat warmer

Webster In World War II, in the Army the commanding officer of the unit was held personally responsible for the foot injuries from cold among his men. He was the one who was censured rather than the private, and there foot discipline became quite effective.

Schuman I will say this, that the regard in which the British soldier holds his lance corporal seems to be much higher than that which our trooper holds for his own sergeant. I do think, from personal observation, that a lot of the foot hygiene and the so-called command responsibility was a little bit better in the British Army than it is in our own experience. This latter aspect was not surveyed, however and remains an impression only Of course, command responsibility can be carried to the extreme and cases can be run underground.

Meryman In some of the trips that I made into South Korean locations I got the impression that they had just about as much frostbite as we did but they never evacuated anybody I saw quite a number of people with lesions easily as bad as the ones that our men had, but they stayed on the line and ignored them.

Schuman The largest amount of data we have on troops of other nationalities other than the British are for the ROK troops. It was interesting to explore the possibility of an acclimatization factor operating among them. We actually saw a lot of youngsters almost naked wandering around in the cold climate, drooling and with mucus running from their noses. It was a common belief among the GIs in the theater that these people hardened themselves that way but, actually for the number of troops that the Koreans had along the lines, they too, had their share of cold injuries. However their total incidence as calculated does not compare with ours. Theirs was lower I was interested to see what their diagnoses were like. I don t think that their hospitals ever saw a first degree frostbite at all. Their hospitals saw but a small portion of their second degree cases and their 200 odd cases represent, for the most part, third and fourth degree injuries. For that reason, we did *not* make a mathematical comparison because there could be no valid comparison there. Their judgment of degree was different and what they were feeding into the line of evacuation was different. It was, thus, impossible to find out the true incidence among them. Speculating, however on the degrees of injury represented and correcting for total strength of divisions in actual combat, we arrive at a rate which is not much unlike ours.

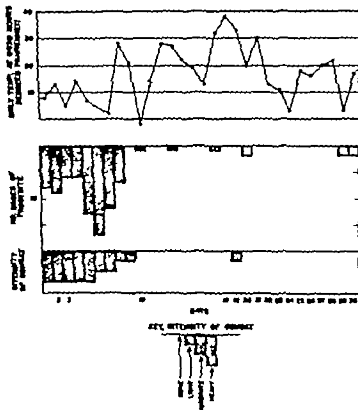


FIGURE 3. The relationship between the daily number of cases of frostbite with an estimate of daily combat action and daily temperature taken at 6:30 a.m. This is within a single unit on 30 consecutive days. Reprinted, by permission, from Orr, K. D., and Fainer, D. Cold injuries in Korea during winter of 1950-51. *Medicine* 31: 177 (1952).

Figure 3 indicates the relationship between combat activity, the low temperatures, and the incidence of frostbite. This was a measure of those relationships in a single army unit and shows the important role of combat activity.

We were interested in the precise relationship between the agent, cold, and the incidence of cold injury. This was one of the problems which remained unanswered at the end of World War II. First, we wanted to find out whether there was a better measure of correlation between the incidence of cold injury and average temperature, minimum temperature or wind chill. Figure 4 shows a fair

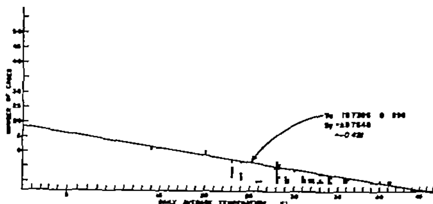


FIGURE 4. Relationship between daily incidence of cold injury and daily average temperature, *Entire U.S. Front, Korea, 1951-52.*

correlation (product moment) between the average daily temperature across the entire United States front in Korea and the incidence of cold injury Each dot represents a separate day We were able to calculate a definite regression line and get a standard error of estimate of approximately 9 cases plus or minus.

We wondered about the rectilinearity of this curve and what effect combat activity had in this particular correlation. We saw that some of these plotted points were seemingly out of place. When we went back to the original data of the daily incidence we found, as shown in Figure 5 that the five points that are circled represent the five days of intensive combat activity at the end of November when the first cold spell occurred, and when three or four of these units were caught without their shoepacs and were hit by the enemy at the same time. Removing these five points does two things to the curve It improves the correlation to a level worth while considering and, it reduces a standard error of estimate from nine cases to five so that you obtain a level of predictability which is relatively good. We can with this kind of regression line for a stable set of conditions, namely a static defense front and adequate gear begin to make predictions of incidence. To show further what this removal of the five points actually does, the efficiency of prediction goes up from 9 per cent to 20 per cent which is an even better measure than the rise from −0 431 to −0 627 in the coefficients of correlation.

There is another point that seems a little out of place and that is the 40 cases at 16° F That proved to be January 12 where the

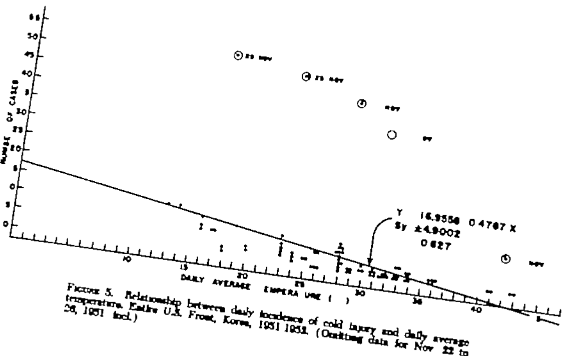


FIGURE 5. Relationship between daily incidence of cold injury and daily average temperature, Entire U.N. Front, Korea, 1951-1952. (Omitting data for Nov 22 to 28, 1951 incl.)

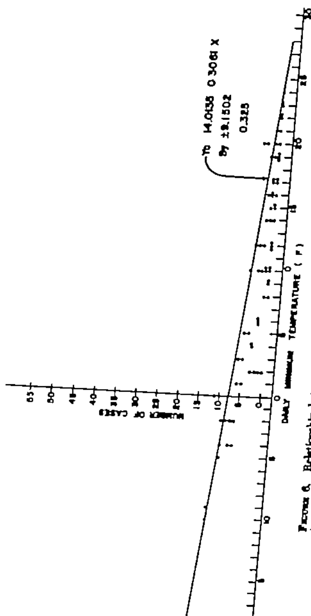


FIGURE 6. Relationship between daily incidence of cold injury and daily minimum temperature, Entire U.S. Front, Korea, 1951-52.

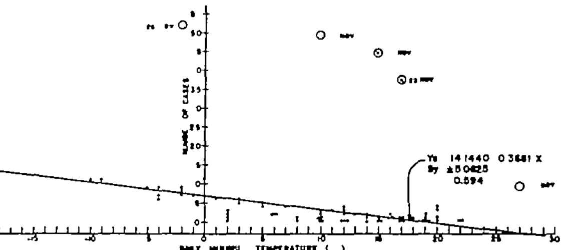


Figure 7 Relationship between daily incidence of cold injury and minimum daily temperature. Entire U.S. Front, Korea, 1951-1952. (Omitting data for Nov 22 to 28, 1951 incl.)

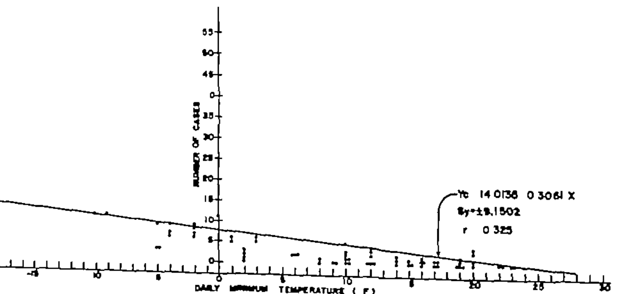


FIGURE 6. Relationship between daily incidence of cold injury and daily minimum temperature. Entire U.S. Front, Korea, 1951-52.

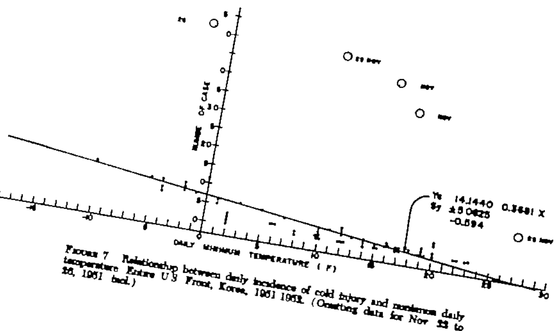


FIGURE 7 Relationship between daily incidence of cold injury and minimum daily temperature. Entire U S Front, Korea, 1951 1952. (Omitting data for Nov 23 to 26, 1951 incl.)

Schuman No we have not yet tested the curvilinearity of these particular data.

An identical procedure was applied utilizing wind-chill data to obtain a regression line for the data (Figure 8) with the days of heavy combat included, and also (Figure 9) omitting the days of heavier combat to obtain a more nearly uniform base. Actually these correlation coefficients for average and minimum temperatures and for wind-chill are not significantly different from each other and if this type of data is to be utilized in prediction of cold injury I would say that one should accept that variable which can itself be predicted reliably for average temperatures and wind-chills are retrospective values and not predicted values as is the next days minimum temperature. Thus, the minimum temperature which is predictable by previous evening dew points lends itself for application to such equations of prediction. Figures 4 to 9 inclusive, presenting data for terrain like Korea and for the kind of combat that was engaged in are included as a possible clue to future analyses of this type. I personally believe that this is worthy of further exploration for prediction in all types of combat activity

Because of the contributing modifying factors, such as combat activity the type of gear individual susceptibility possible differences in racial susceptibility and so on, it is surprising that there is any kind of correlation at all between the relationship of duration and intensity of exposure to the degree of injury Table III is presented to indicate a possible further attack on the problem. The longer a person is exposed to cold the greater is his likelihood of cold injury also the lower the temperature the greater is his likelihood of frostbite. By multiplying the two elements, namely the duration of exposure and the reciprocal of the temperature, an exposure index is obtained. The values which are presented in Table III are not, unfortunately significantly different from each other degree by degree, when tested at 5 per cent probability levels by the t test, but this is a possible clue to future work because there does appear to be a trend in the direction of increasing mean exposure indices with increasing degrees of injury If, in some future theaters of war the temperature range is lower I believe that one would have to use the absolute temperature scale to get below the negative values that might then be dealt with or add some constant that could overcome that negative value. In any event, such indices are relative and must be calculated identically for comparison. It is possible that one factor contributing to the failure to elicit significant increases in the exposure index with increasing degrees of

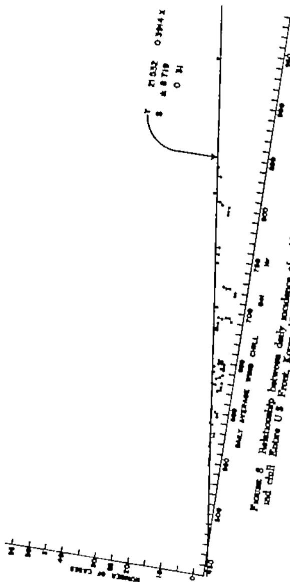


FIGURE 8 Relationship between daily incidence of cold injury and daily average wind chill Entire U S Front, Korea, 1951-52

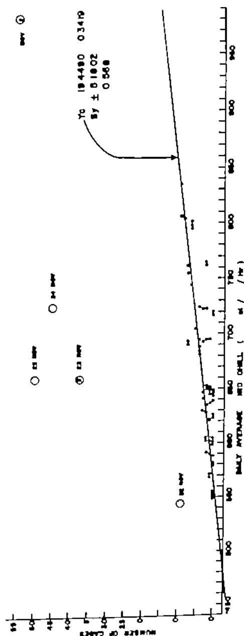


FIGURE 9. Relationship between daily incidence of cold injury and daily average wind chill. Entire U.S. Front, Korea, 1951-52. (Omitting data for Nov 22 to 26, 1951, incl.)

TABLE III

Exposure Indices for 298 White and 208 Negro Cases of Frostbite of the Feet and Hands, Korea 1951-52

Degree of Injury	Exposure Index					
	White			Negro		
	No	Mean	Standard Deviation ±	No.	Mean	Standard Deviation ±
1	138	0.73	1.78	74	0.50	0.94
2	96	0.81	1.14	64	0.76	1.58
3	52	0.91	1.11	58	0.42	0.43
4	12	0.93	1.10	12	0.85	1.23
Total	298	0.79	1.47	208	0.58	1.11

D=Duration of Exposure in Hours.
T=Minimum Temperature of Exposure in Degrees F
$E.I. = D \frac{1}{T}$

injury is the classification of the degree of injury itself Our present classification fails to account for total area of involvement.

Burton It would seem to me more reasonable instead of using the inverse for temperature to use the difference of the actual temperature from some temperature which causes no injury say 40 F It would seem to me that logically it couldn't be anything to do with the inverse of the temperature. What matters is how much colder it is than an innocuous temperature, and it might be worth trying that.

Schuman Yes, that is a worth while suggestion. Our theory or hypothesis was next applied to the data for the Negro Again, there is no significant difference between the degrees of injury Between the values of 0 76 and 0 42, there is a significant difference but in light of the balance of the data, this may be chance. Of interest, however is the trend for the white patients to have a higher index of exposure than the Negro though not significantly so statistically Thus trend was also suggested by some of our other data but the Negro was exposed for similar periods at somewhat higher temperatures than the white to obtain the same kind of injuries

Horvath It is only your third-degree injuries which show any significant differences, at least just from looking at the figures. I don t think there is any difference at all in the first-degree or the fourth-degree between those two groups.

Schuman That is correct. There are no significant differences there by rigid statistical tests but there are trends. This is the collective experience, irrespective of climatic region of origin. The statistical significance which lies between the two values for third-degree injuries, as Dr Horvath pointed out, may be a chance occurrence. I mentioned the racial difference because in the data for temperature of exposure alone, there is a difference between the white and the Negro in other words the average temperature for the Negroes is significantly higher than the average temperature for the whites.

Horvath Is this duration of exposure in hours obtained from your questionnaire of these people?

Schuman Yes. This is obtained from the time, for example, that patients went out on patrol. It was just from the time they were first immobilized until the time they re-warmed by whatever means, walking, or fire, and so forth.

Horvath If they were pinned down for an hour say but it had taken them five hours to get there, the five hours were not considered?

Schuman The five hours of walking to their particular patrol were not considered.

Burch What is an average value for D?

Schuman The average value was about 7 hours for the entire experience. There is a wide range in exposure times. There was anywhere from 2 or 3 hours to 12 or 18 hours. In some of the patients who were on outposts without heat, and who were under enemy observation, there could not be more than slight movement for upwards of almost a day at times.

Burch Did you make any effort to estimate the number of calories of heat that could be lost with the temperature gradients involved in your studies? It would require a fairly long time for a leg to cool to a freezing level and the rate of cooling should be expressed in terms of calories per hour per kilo of limb.

Schuman: No

Burch It appears to me that if freezing takes place in two hours, that might be too short for it to reach deep levels. You could estimate the accuracy of your data by such a study

Schuman That is obviously the difficulty here, because, so far what has not been done is to separate these people on the basis of their previous exposure to cold inside the bunker before going out on patrol. I believe it should be done in future studies of this kind, and comparisons made between those who came from a heated bunker and those who did not, and were virtually exposed for the same length of time, on the same patrol.

Horvath That may be the difference, why they got frostbite or did not get frostbite.

Siple The thing I would suggest which might be of much greater importance, on these patrols is the state of their clothing, whether dry or damp with sweat, at the time they began to get their exposure.

Horvath That would be related to the same fact. There is a fairly decent tangible or factor involved, I think, which is related to moisture but at the same time it is related to the previous status and the duration of total exposure that the man had. That is why I think there is no difference between any of those at the present stage even regardless of what you use as your corrective factor or your index. Theoretically I would say it doesn't matter how long you are there. It is the type of injury you get. There simply must be some relationship between the injury you get and the exposure, because of all these modifying factors.

Crismon One very slippery criterion is this matter of numbness. What justifies that contention is the frequency with which the injury was discovered only after the boots were removed, even the next day. The injury period and the period of numbness had entirely escaped the attention of the individual for one reason or another because he was being shot at at the time, he really did not notice the injury until he saw the blister on his toe.

Schuman Table IV presents a provocative problem. At the end of World War II, there were just isolated experiences in which there was some indication that other races were more susceptible than the white. In the 1950-51 experience, Colonel Orr and Captain Fainer also noticed a preponderance of cases among Negroes in their total experience. However a portion of this particular phenomenon was obscured by the fact that there were solid Negro regiments involved, and that a true racial factor did not contribute as much as did all the other modifying factors in the situation. Whayne mentions a regiment which experienced a high attack rate in comparison with other regiments but that was the only

TABLE IV

Distribution of 716 Cases of Frostbite and 455 Bunker-Mate Controls According to Race, Korea 1951-52

Race	Cases		Controls	
	No.	%	No.	%
White	417	58.2	407	89.5
Negro	291	40.6	37	8.1
Mongol	8	1.1	11	2.4
Total	716	99.9	455	100.0

example which was cited in World War II. The difficulty in World War II was that the majority of Negro troops were held in service organizations rather than in front line positions. In Korea, in the winter of 1951-52, the situation was entirely different from what it has been in the history of American combat troops. There was approximately from 9 to 10 per cent distribution of Negroes in the front-line units throughout the entire front.

With that kind of situation one has the stabilizing or correcting factor of distribution as far as morale, training, individual combat experience and many other features are concerned.

Horvath Except that you had the intangible of from 1 to 10. There is an individual who is still distinguished by color from the others.

Schuman Exactly However from personal observation, which is not a measurable quantity and which I do not present as proof, the relationship between Negro and white in the combat zone, on the front line especially is one, I think, virtually without any discriminatory practice. I have seen white boys taking commands from Negro sergeants I have seen white boys being run through the paces of mortar practice with a Negro corporal giving the commands or firing directions etc. I have seen, and this is pertinent to an understanding of this problem, a Negro boy asking a white boy to wait for him and not to leave him behind in a given particular problem, and the white boy saying, "I'll sure be there, Bud. There was the tie of a common emergency that was present in this group How to measure that, I don t know But it was my impres-

sion from personal contact with these men that any discriminatory practices were virtually nonexistent on the front lines.

With *all* these intangibles in mind, it is still of interest that the Negro showed this disparity in the incidence of cold injury. They represented but from 9 to 10 per cent of the total combat elements and yet 40.6 per cent or 41 per cent of the total incidence of frostbite, (Table IV) occurred among Negroes.

Burch Is it your impression that Negroes do or do not develop frostbite as readily as whites?

Schuman It is my impression, which I will try to develop that they get it faster and more often.

Burch Is it your impression that it is due to susceptibility of the Negro tissue to freezing?

Schuman I am going to present all the evidence for and against that and let you gentlemen decide, on the basis of the evidence. With all the factors that we have evaluated thus far and until proved otherwise, I think there is a racial difference.

Burch: In tissue susceptibility?

Schuman Possibly

Burch Could it not be habit, environment or learning?

Schuman I don t know Perhaps we had better not use the word, susceptibility

Kark What about their educational background? From my experience with Negro students at Meharry Medical College, the difference between teaching those students and teaching white students was not that they were not able to work just as well as the white students but that they were limited by reason of an inferior educational background in their secondary and high school years. I wonder whether you made any breakdown in that regard?

Schuman We made it on the basis of the Army General Classification Test scores in Areas I and III. It is about the closest approach to a combination of intelligence and learning tests, that we have.

Shumacker: Don't you think that the circumstances under which these men were injured would tend to minimize the opportunity for differences in educational background to come into play? Front line fighting is a pretty primitive sort of existence and the measures that can be taken to prevent cold injury are relatively simple ones.

Schuman To change a pair of socks is not necessarily an achievement of high intelligence. That is what I would like to bring out, too.

Kark Well, of course, but that isn t what I am trying to bring out now It seems to me that in protecting oneself from the cold, in being indoctrinated to protect oneself from the cold, one goes through a whole process of learning to do it satisfactorily All of us who have lived in the cold learn to watch each other If you pair off you do better than if you don t pair off It may be that you have some block in being able to do a protective job well, because of your previous background and education as a youngster. I mean your attitudes. The only point I wanted to make is that it is very hard to say what effect your early educational background has on your rate of learning new phenomenon, or your ability or desire to learn.

Meryman How about the breakdown, if such exists on these cases on the use of equipment, which would be a reflection of this intelligence factor? If a percentage of the cases resulted from a man losing or misusing his equipment, that certainly is not a physiological factor and would to some extent be dependent on his intelligence, his ability to learn.

Horvath Yes How many of these frostbites were due to the fact that a man was holding a gun barrel or sitting on a tank and got his bottom scraped off that way?

Schuman There were relatively few tank cases, relatively few cases of hand frostbite. There were a few hand cases that had their origin in removal of gloves to unjamb weapons, but they do not represent the bulk of these cases which were primarily of the feet.

Adams Ray Kristian Stray (3) has been making an investigation of susceptibility to cold among Norwegian troops and he has found a difference between blondes and brunettes

Shumacker Commander Schuman, do you have information about when socks were changed?

Schuman Yes, I have.

Shumacker I have the impression that when studies have been carried out to determine possible differences between Negroes and whites in aptitude for learning, they have shown that no essential differences are evident at the level of primitive intellectual processes. For example, I believe it has been shown that no differences are noted at the beginning of school. They are apt to become evident when content becomes an important factor The child is better off then if he has a good family background which has provided him with some understanding of such things as history geography and literature. Though I may be wrong about it, I think we are con-

cerned with primitive learning habits rather than more complicated ones, such as are of importance to the medical student.

Kark What about personal discipline? That is the thing. Personal discipline is something that you learn early in life, in the bosom of your family and in school. What I am pointing out is that one would like to know whether the educational background of these groups was comparable in their early years. I don't think you can get that data very easily

Meryman In talking to these frostbite patients when they have been evacuated, I had the impression that there were many episodes in which the ultimate injury could have been prevented if the fellow had only used his head, and that stupidity whether from excitement, preoccupation, or innate in the individual, had prevented him from taking the proper course. I still feel that this should be a very important aspect.

Horvath My impression from watching Negro troops and white troops up in Canada during the war was that although we did actually see a slightly greater number of Negro troops with frostbite than we did of white troops, in many cases some of the accidents with the Negro troops were deliberate in that particular situation. I am not too sure, actually as to whether this is a real difference you measured or whether this just happens to be something in the data which suggests that difference. I know for instance, when we came back from that experience in Canada, we put a group of 80 whites and 30 Negroes on a simple test of exposure to low environmental temperatures and then followed their skin temperature response, and, frankly it was impossible to distinguish between the two groups, as far as I could tell. The toe temperatures of the Negroes would go as low as they would in the white. The rectal temperature rises and falls were essentially equivalent. Their survival or their responses for three hours in −20 or −40 C. seemed to be the same. There may be a difference, but I would be somewhat hesitant in putting forth a statement of difference until I have had at least more information.

On the basis of the initial chart that you have and your developed ratio, I can't see that it is possible to suggest any difference. You have one set of statistical data saying there is a difference and another set of statistical data saying there isn't any difference. Table IV illustrates a distinct difference in incidence between the races whereas Table III relates duration and intensity of exposure to degree of injury for the two races and does not demonstrate differences in attack rate. Table IX reveals that there are certa

differences between the races which may or may not contribute to the difference in incidence However attention is directed to the item of temperature of exposure which is definitely higher for the Negro than for the white and is a component of the exposure index itself

Shumacker If the same sort of data is brought out in the rest of the discussion, it will demonstrate a real difference in incidence regardless of whether this is explainable upon some difference in intrinsic racial susceptibility or upon differences in behavior From the practical standpoint, this should be of enormous value to the Armed Forces in planning maneuvers and campaigns in cold regions.

Horvath On the basis of the essential details is this just a figment of our data or is it a figment of our imagination or is it a true fact, that there is a physiological difference between these two races?

Schuman It is the purpose of this presentation first to demonstrate that there is an observed difference and then to attempt an analysis of the factors that may be contributing to that difference. Probably the use of the word susceptible is unwise at the present time and caution should be exercised in its use in connection with these racial differences. But there is a real difference here which I think Dr Shumacker and Colonel Orr have mentioned and the "why of it, of course, is what we are going to try to ferret out.

Now Table V demonstrates in more concrete form the relative risk of attack by race when one considers the strength of the Eighth Army all the divisions and all the regiments according to race. Then, as was done in relation to echelon groupings (Table I) the same type of calculations was made for racial strength in the divisions and in the regiments. Individual racial attack rates per thousand are shown and then finally the ratios between races for the several echelons. It will be seen that the Negro was attacked approximately from four to six times as frequently as the white on the basis of strength in the Eighth Army The ratio for the Eighth Army as a whole, was from 1 to 4 for all the divisions from 1 to 6½, and for all the regiments from 1 to 6 The larger ratios for division and regiment are immediately apparent because of the difference in percentage distribution of the basic population by race in divisions and in regiments as compared to the Eighth Army *per se* In other words, this would indicate that there are still more Negro troops used as service troops and support troops than in more or less combat levels or echelons

In demonstrating these risk-of-attack ratios among the Negroes and the whites on the basis of climatic region of origin, we come

TABLE V

Comparison of Total Frostbite Attack Rates and Relative Risks of Attack for the Several Echelons of the U.S. 8th Army According to Race, Korea 1951-52

Race	Percentage			% of 8th Army Racial Strength	% of Division Racial Strengths	Total Attack Rate per 1000 Strength			Relative Risk of Attack		
	In 8th Army	In Div	In Reg	In Div	In Reg.	In 8th Army	In Div	In Reg.	In 8th Army	In Div	In Reg.
White	85.6	91.0	90.1	50.1	59.1	2.10	3.97	5.80	1.00	1.00	1.00
Negro	14.4	9.0	9.9	29.6	65.5	8.65	25.91	35.86	4.12	6.53	6.18
Total	100.0	100.0	100.0	47.2	59.7	3.04	5.95	8.78	1.00	1.95	2.85

up with the particular values shown in Table VI. In order to adjust the attack rates according to the population, one does the usual weighting of these values by multiplying by the reciprocal of the particular percentage that we find.

TABLE VI

Comparisons of Relative Risks of Attack by Frostbite Between White and Negro Populations of the U S. 8th Army Korea 1951-52

Region and Race	% in 8th Army ( ) (Pre-Exposure Sample)	No. of Cases (b)	Adjusted Case Rate (b × 1/)	*Risk of Attack Ratios	
Northern White	32.6	113	346.57	1 000	1 000
Southern White	52.8	295	558.78	1.612	
Northern Negro	0.9	24	2666.66	7 694	5.053
Southern Negro	13.7	262	1912.34	5.518	
Total	100.0	694	—	—	—

Because we had only the pre-exposure sample as the source of data as to the state of origin of the white and Negro troops, we used this pre-exposure sample as the criterion for the distribution in the Eighth Army as a whole. By other tests, we showed that the pre-exposure sample was very representative of the Eighth Army for several other criteria which were used. Rank and race fell in the same percentage pattern. When the adjusted case rates, which in themselves are only indices and not actual values, are related one to the other we note, a repetition of the average ratio noted before, about five times the attack rate among Negroes as among whites, and when we consider the regional differences we find that the southern white is significantly different, from the northern white, in that they have 1.5 to 1.6 times the attack rate. There is, however no significant difference between the northern and southern Negroes, even though there is a greater numerical difference between them. The standard deviation of the value of 24 cases for the northern Negro was large.

If the Negro is more commonly attacked, according to this particular hypothesis, the Negro should show more high-degree injuries than the white man if he is more susceptible again per

TABLE VII

Relation of Degree of Injury to Region of Origin and Race Among 336 White and 236 Negro Cases of Frostbite of the Feet, Korea 1951-52

Race	Degree of Injury – Feet										X^2	P
	1		2		3		4		Total			
	No.	%	No.	%	No.	%	No	%	No.	%		
Northern White	41	43.2	32	33.7	18	18.9	4	4.2	95	100.00	0.4674	>.90
Northern Negro	6	35.3	6	35.3	4	23.5	1	5.9	17	100.00		
Southern White	117	48.5	75	31.1	39	16.2	10	4.1	241	99.9	16.5060	<.001
Southern Negro	77	35.1	62	28.3	68	31.1	12	5.5	219	100.0		
Total White	158	47.0	107	31.8	57	17.0	14	4.2	336	100.0	16.8290	<.001
Total Negro	83	35.2	68	28.8	72	30.5	13	5.5	236	100.0		

mitting the use of the term in the sense of factors operating to produce greater injury We find (Table VII) that in comparing the northern white cases of foot injury with those for the northern Negro there is no significant difference in the two curves of distribution by the chi-square test, but no reliability can be placed upon this value as it deals with chi square cell values less than five. However examining the more adequate data for the southern white as compared to the southern Negro we do find a reversal. You will notice that whereas the southern white has 48.5 per cent of the injuries in the first degree and the southern Negro 35 per cent, there is an approach to equivalence in second degree and then a reversal in the third and fourth degrees combined. We find a higher rate of higher-degree frostbite among the Negroes as compared to the whites. This is indicative of some difference operating. The significance of the chi-squares is pretty high and, for the total group, it remains as such despite the paucity of the northern Negro cases.

That was true for feet. The same thing applies to the distribution of severity or degree of injury for the patients with injuries of the hand as well (Table VIII) For the northern white and northern Negro comparison, there does not appear to be any significant difference in the distribution. We are dealing again with very small numbers and I don t think this is very reliable, even in the chi-square application. For the southern white compared with the southern Negro, however there is a significant difference, and for total experience the same is true.

Kark Of the 24 northern Negroes represented in Table VI, how many had been brought up in their childhood in the South?

Schuman None. Actually in determining the region from which they came, we took the state where they spent the greatest number of years of their life as the state of origin for that particular individual.

Kark I am concerned with early education. We have been able to notice a difference in many ways in the Negro, as we see him at the hospital in Chicago between those who have been reared in their childhood in the South and those who lived in Chicago.

Schuman The locale of early education was not checked, in other words, whether or not they had lived in the South first or last. When they were asked what state they came from as well as the collateral questions of "How many years did you live there?" "When did you live there?" "What part of your life?" etc., we did not, of course, then tabulate or put down the data according to where they had had their early education. In other words, some of

TABLE VIII

Relation of Degree of Injury to Region of Origin and Race Among 104 White and 74 Negro Cases of Frostbite of the Hands, Korea 1951-52

Race	Degree of Injury – Hands										X^2	P
	1		2		3		4		Total			
	No.	%	No.	%	N	%	No	%	No.	%		
Northern White	13	59.1	5	22.7	2	9.1	2	9.1	22	100.0	4.7490	> .10
Northern Negro	3	37.5	5	62.5	—	—	—	—	8	100.0		
Southern White	44	53.7	31	37.8	2	2.4	5	6.1	82	100.0	9.9365	< .08
Southern Negro	23	34.8	31	47.0	9	13.6	3	4.5	66	99.9		
Total White	57	54.8	36	34.6	4	3.8	7	6.7	104	99.9	10.3528	<.02
Total Negro	26	35.1	36	48.6	9	12.2	3	4.1	74	100.0		

these people could have been born in a southern state and moved soon after to the North and they would be classified as northern, or of northern origin

Kark I would agree with that, but one who has been brought up to the age, say of ten or twelve, in the South, I wouldn't consider him a northern Negro

Schuman No, we did not. You see, ten years was really the cutoff point Where he spent the greatest number of years of his life determined his state of origin.

Kark I would say I am thinking about the early part of their lives, the most important in terms of personal discipline. If they spent six years growing up, say in Nashville Tennessee, I would consider them at the age of eighteen as probably southern.

Schuman Usually they come directly from their places of birth into the Army In the pre-exposure data we tested for the number of people who moved from one region to another and the percentage was very very low These boys seemed to come directly into the Army from the region in which they had spent the greatest part of their lives. In the few instances where there was migration, we did record the state of origin as the place in which they had lived the greatest length of their lives, rather than the last place where they had lived.

Burton On this question of cultural and behavioral differences, possibly due to early education which Dr Kark raised, my own view would be that although it is true that the level of indoctrination is perhaps a primitive level, so that the previous education of whites and Negroes enabled both of them to take it in, the real thing that determines whether one keeps out of trouble in the cold is not so much a slavish following of rules but following them intelligently and being willing to make exceptions, because no set of rules can cover all the cases and circumstances that one has to meet. One has to act intelligently and take the initiative in modifying a rule. In other words, you may be told to change your socks once or twice a day and it seems to me that the Negro because of sociological reasons as much as educational, is inclined to stand back and be told and follow exactly the rules that he has been given, whereas the white is willing to take the initiative and modify the rule and not change his socks when it is 40 F below and get his feet frostbitten as he did it. I think there may be a very real difference there, in spite of the fact that the level of intelligence and previous education required for taking this indoctrination is at a primitive level. I think that keeping efficient in the cold depends

on a more intelligent application of the rules of indoctrination, and I think indoctrination is not enough. It is the experience with cold that you have to add to it. It is because of this reason, isn't it, that we have to have the experience? I think I am inclined to agree that this may be a real educational-cultural-sociological initiative difference.

Burch I think there is another factor here which is against differences due to tissue constitutional or genetic factors, e.g., you found the southern white and the northern white to be different. I would not expect genetic or constitutional differences to exist between those two groups. I would think that experience in protecting oneself in the cold might be a factor

Schuman In analyzing each of the factors in Table IX, we found, first of all, that the Negro was just about 0 4 of a year younger than the white, and though that difference was shown to be statistically significant, I do not place a great amount of importance on that particular difference. I don't know how much a one-half year difference in age is going to make as far as schooling is concerned or as far as maturity at this particular age level is concerned. The whites did significantly outrank the Negro – but the question of promotion rate which arises cannot definitely be answered. The total number of white sergeants, who were frostbitten as compared to the Negroes did not show any great difference. These differences in Table VIII do represent differences between privates first class and corporals for the most part, because the total number of sergeants frostbitten was relatively small.

The question arose whether rurality or urbanity of previous existence played any role in predisposition to frostbite. It can be seen that the type of residence did not seem to be different between whites and Negroes.

If frostbite is a matter of training and experience, troops who have been in Korea longer should be more hardened and more experienced in their combat life and therefore should be less prone to frostbite. For some reason, unexplained at the moment, the Negro patients seem to have been in Korea approximately thirty days or a month more than were the whites A statistically significant difference. But if one raises the question, "Well, what does this mean by way of fatigue?" one has only to refer to the number of days in combat without rest, to find that there is no significant difference between the races, so that the physical fatigue factor does not seem to play a major role here.

these people could have been born in a southern state and moved soon after to the North and they would be classified as northern, or of northern origin.

Kark I would agree with that, but one who has been brought up to the age, say of ten or twelve, in the South, I wouldn't consider him a northern Negro

Schuman No we did not. You see, ten years was really the cutoff point. Where he spent the greatest number of years of his life determined his state of origin.

Kark I would say I am thinking about the early part of their lives the most important in terms of personal discipline. If they spent six years growing up, say in Nashville Tennessee, I would consider them at the age of eighteen as probably southern.

Schuman Usually they come directly from their places of birth into the Army In the pre-exposure data, we tested for the number of people who moved from one region to another and the percentage was very very low These boys seemed to come directly into the Army from the region in which they had spent the greatest part of their lives. In the few instances where there was migration, we did record the state of origin as the place in which they had lived the greatest length of their lives, rather than the last place where they had lived.

Burton On this question of cultural and behavioral differences, possibly due to early education, which Dr Kark raised, my own view would be that although it is true that the level of indoctrination is perhaps a primitive level, so that the previous education of whites and Negroes enabled both of them to take it in, the real thing that determines whether one keeps out of trouble in the cold is not so much a slavish following of rules but following them intelligently and being willing to make exceptions, because no set of rules can cover all the cases and circumstances that one has to meet. One has to act intelligently and take the initiative in modifying a rule. In other words, you may be told to change your socks once or twice a day and it seems to me that the Negro, because of sociological reasons as much as educational, is inclined to stand back and be told and follow exactly the rules that he has been given, whereas the white is willing to take the initiative and modify the rule and not change his socks when it is 40 F below and get his feet frostbitten as he did it. I think there may be a very real difference there, in spite of the fact that the level of intelligence and previous education required for taking this indoctrination is at a primitive level. I think that keeping efficient in the cold depends

The number of days in combat are associated with the days in Korea a little more closely than the number of days in combat without rest. There was a significant difference here also, but it is opposite to that which one would expect if the question of difference in experience were involved to account for racial differences.

The Negro did not differ materially from the white in his history of previous cold injury For a history of previous cold injury we took any history in which there was at least evidence of exposure to cold, numbness and tingling upon rewarming and subsequent desquamation, not the ordinary numbness that we all report. We did go so far as to ask, "Were you hospitalized for it?" If not, "Did you see a doctor for it?" "Did your skin peel?" If they claimed they peeled, we included them as having had a history of previous cold injury

The whites and Negroes differed on the basis of history of previous illness only with respect to syphilis. The inquiry of previous illnesses was part of the questionnaire as a possible clue to the production of cold hemoagglutinins. This was used primarily as a possible factor of predisposition to cold injury on the basis of some of these diseases. What role syphilis plays in cold injury I am not prepared to say From our knowledge of the attack rates in venereal diseases among the Negroes as compared to whites, this is not an untoward finding.

The amount of smoking which these people did was necessarily limited for the most part by the amount of cigarettes distributed to them. They received a ration of a pack a day but there was a certain amount of swapping of packs. Some people did not smoke and swapped their cigarettes with those who did smoke for other items such as food or chocolates. The amount of cigarettes smoked by the white and Negro is significantly different statistically What, however does 0.2 of a pack less for the Negro actually mean?

Usually troops ate just before going out on a combat patrol. These values, not different at all virtually are in line with the length of combat patrols for the most part, which did contribute the greatest bulk of the cases as far as activity was concerned. It is noted that the interval was 7 9 hours for the Negro patients and 7 7 hours for the white. There is nothing here to indicate an environmental or host factor difference.

The item, content of the last meal, was based on whether they ate B ration or C ration, native food, or some of the other types of food packs. We used the minus and plus signs to show any slight differences in one group or the other irrespective of their significance.

TABLE IX

Summary of Analyses of Factors Tested for Relation to Frostbite, In Regard to Race, Korea 1951-52

Item	Race		Test of Significance	Value	df	P
	White	Negro				
Mean Age (Yr.)	22.0	21.6	t	2.352	694	<.02
Rank	+	—	χ^2	29.616	4	<.001
Type of Residence	Rural	Urban	χ^2	8.321	1	>.05
Days in Korea	93.7	120.9	t	5.779	661	<.001
Days in Combat	46.2	62.6	t	4.704	670	<.001
Days in Combat without Rest	16.0	16.6	t	0.515	656	>.60
Previous Cold Injury	+	—	χ^2	5.413	3	>.10
Previous Illness (Syphilis)	—	+	χ^2	24.436	7	<.001
Smoking (Packs)	1.1	0.9	t	4.369	556	<.001
Hours Since Last Meal Eaten before frostbite	7.7	7.9	t	0.443	661	>.60
Content of Last Meal	—	+	χ^2	4.621	4	>.30
Footgear Worn	+	—	χ^2	3.120	6	>.70
Extra Footwear Carried	+	—	χ^2	1.420	4	>.80
Average Change of Socks (Days)	1.5	1.7	t	2.234	552	<.05
Average Change of Innersoles (Days)	1.3	1.5	t	0.802	258	>.30
Last Change of Socks	1.1	1.2	t	1.692	563	>.05
Sockgear Worn	+	—	χ^2	21.060	6	<.01
Sockgear Footgear Comb. Constrictive	+	—	χ^2	0.654	3	>.80
Inadequate Insulation	—	+	χ^2	6.195	4	>.10
Condition of Feet (Dry)	—	+	χ^2	8.163	4	>.05
Handgear Worn (Gloves)	+	—	χ^2	8.949	6	>.10
Condition of Hands (Dry)	—	+	χ^2	1.956	8	>.70
Activity	+	—	χ^2	10.170	8	>.20
Average Minimum Temp. of Exposure	11.7	13.6	t	2.150	620	<.03
Personal Hygiene	+	—	χ^2	43.905	2	<.001
AGCT Score Area I	92.5	73.2	t	4.534	71	<.001
AGCT Score Area III	92.2	73.2	t	4.186	71	<.001

The number of days in combat are associated with the days in Korea a little more closely than the number of days in combat without rest. There was a significant difference here also, but it is opposite to that which one would expect if the question of difference in experience were involved to account for racial differences.

The Negro did not differ materially from the white in his history of previous cold injury For a history of previous cold injury we took any history in which there was at least evidence of exposure to cold, numbness and tingling upon rewarming and subsequent desquamation, not the ordinary numbness that we all report. We did go so far as to ask, "Were you hospitalized for it?" If not, "Did you see a doctor for it?" "Did your skin peel?" If they claimed they peeled, we included them as having had a history of previous cold injury

The whites and Negroes differed on the basis of history of previous illness only with respect to syphilis. The inquiry of previous illnesses was part of the questionnaire as a possible clue to the production of cold hemoagglutinins. This was used primarily as a possible factor of predisposition to cold injury on the basis of some of these diseases. What role syphilis plays in cold injury I am not prepared to say From our knowledge of the attack rates in venereal diseases among the Negroes as compared to whites this is not an untoward finding.

The amount of smoking which these people did was necessarily limited for the most part by the amount of cigarettes distributed to them. They received a ration of a pack a day but there was a certain amount of swapping of packs Some people did not smoke and swapped their cigarettes with those who did smoke for other items such as food or chocolates. The amount of cigarettes smoked by the white and Negro is significantly different statistically What, however does 0.2 of a pack less for the Negro actually mean?

Usually troops ate just before going out on a combat patrol. These values not different at all virtually are in line with the length of combat patrols for the most part, which did contribute the greatest bulk of the cases as far as activity was concerned It is noted that the interval was 7.9 hours for the Negro patients and 7.7 hours for the white. There is nothing here to indicate an environmental or host factor difference

The item, content of the last meal, was based on whether they ate B ration or C ration, native food, or some of the other types of food packs. We used the minus and plus signs to show any slight differences in one group or the other irrespective of their significance.

In other words, the Negro seemed to eat a little bit more of the hot meals, or more of the C rations, than did the white. But, again, that difference is not significant.

The white seemed more often although not significantly so, to wear more adequately protective foot gear in other words, he seemed to wear the shoepac more often than the combat boot. But these differences are not at all significant. As to extra footwear there was no difference between the white man and the Negro as to what they carried with them out on combat patrols, on reconnaissance patrols, etc.

The item, last change of socks, however was reliable in the sense that we could corroborate from company commanders and from the sergeants of the squads who were out, the information on when the men changed their socks. It was the practice for them to change their socks before going out on patrol. There was no significant difference between the white and the Negro in this regard.

Type of sock gear worn, taken alone, can be misleading, for it is dependent upon the foot gear worn. Thus, combinations of foot and sock gear were elicited with regard to constriction or inadequate insulation. When broken down in more detail into the constrictive types or the types of combinations which gave inadequate insulation we found no significant difference between the races.

Comparison of the condition of the feet also revealed just the opposite to what would be the case if the excess incidence among Negroes was due to increased wetness The Negro seemed to have a drier foot than the white man. This was not a physiologic observation but merely a question of the individual "Were your feet dry or wet when you reached this particular outpost? Were your feet dry or wet when you reached your objective on this particular patrol?" This was a relative observation on the part of each individual rather than a physiologic determination of sweat that was produced.

Horvath What would be dry for one individual would be pretty wet for another

Schuman That may be true. The hand gear worn was, of course, distributed in the original data according to whether they wore the complete ensemble of glove and insert, or mitten and insert. If they wore both, it was considered adequate. If they wore one or the other it was considered inadequate. On this basis, the white man seemed to show a slight edge over the Negro in wearing adequate hand gear but, again the difference is not significant. The

condition of the hand was drier among the Negroes than among the whites according to their particular personal observation.

Next, we considered activity which was corroborated by the observation of other members of a particular squad in which these patients found themselves. It was, again, very relative. It was graded according to little movement, moderate movement, or considerable movement, and the inquiry was rather carefully made in that a man was asked, "If you were in a bunker was this bunker tall enough for you to get up and walk around or was it just high enough for you to lie down? How many men were in the bunker? Were you able to move from side to side? Were you able to swing around if you were pinned down? Were you able to swing your legs around? Did you have to lie so still that the only thing that moved was your trigger finger?" and so on down the line. It frequently took from twenty minutes to one-half hour to interrogate each of these particular people and get the proper kind of stories out of them so one could place any credence in them. We found no obvious difference in activity between the white and the Negro in respective situations.

The average minimum temperature of exposure was of course, derived by the determination of the meteorologist. Given the period of exposure, the lowest temperature of exposure was determined for that particular individual and the average minimum of each particular group calculated. There is a two-degree difference which happens to be significant. The Negro cases occurred, on the average at temperatures two degrees higher than those to which whites were exposed

Personal hygiene observations were made, for the most part, on pre-exposure controls What the disparity in personal hygiene for the patients themselves may have been on the front lines is unknown. A sampling of patients in the hospital was invalid because this environment did not reflect their status on the front lines. In the pre-exposure study we did have a lot of data on the uninjured troops, with respect to personal hygiene, but I question whether the determination was made in a completely unbiased manner

The scores of the Army General Classification Test in Area I and Area III show differences in these groups. Now these same differences were found in the controls and between North and South. The differences were not significant for the same race between regions but remained significantly different between races in each of the regions.

I personally don't find a great or marked difference between the two groups to account for the disparities in attack except for the

AGCT scores which range from 40 to 146. They seemed to run the same range as we find in the Binet and other intelligence tests.

Meryman That is a fairly significant difference, then.

Schuman It is a highly significant difference. We find the same thing true in the pre-exposure study Is this, then, a contributing factor to the difference between the two?

Webster I assume that these are all African Negroes, or of African origin. Are there any correlations among the other colored troops out there, or isn t there anything in the degree of pigmentation?

Schuman We made no individual observations as to the degree of pigmentation. The Negro group does include Puerto Rican Negroes as well. Some Puerto Ricans were included as whites but actually there were only 30 Puerto Ricans in the whole experience. I don t recall the exact proportion that were Negro and the exact proportion that were white. Do you recall, Ken?

Orr It was approximately 50 per cent.

Siple What was the highest in rank?

Schuman The highest in rank who was frostbitten was a lieutenant of an artillery outfit.

Siple I think we can draw the conclusion from what you have given us that you have exploded at least the possibilities of certain old concepts being true or not being significant. At the same time you have pointed up the ones we need to worry about, even though we have not necessarily found the right conclusive answers yet.

Dugal What would be the correlation between the AGCT score and the incidence of frostbite within the group of Negroes for instance?

Schuman I don't think there was any correlation. If I remember the data, the variations within the pre-exposure controls, who were not frostbitten, and within the group who was frostbitten was large. They showed, as I indicated, the same mean scores with no significant difference between the two.

Meryman One of the things that bothered me about this is the fact that such a large percentage of these men, when you talk to them, have a particular and peculiar circumstance to relate, and that when you are dealing with what is actually a relatively small number of men, a large percentage of them were in some peculiar situation when they received their frostbite. They got snow in their boot, they went through a frozen stream, they were in a truck for a long period of time or some extenuating circumstance. When you add those to a statistical group, why it might just swing it one way

or the other in addition to the fact that to respond to an unusual situation, as Dr Burton points out, is going to require a certain amount of intelligence and initiative.

Schuman This last point, I am not trying to refute. I deliberately presented this data to provoke this kind of discussion, because I do not know the answer However I will take issue with your statement, Harold, that you may vary your statistical analysis by the peculiar circumstance which these people relate. We had controls who were in identical situations, who did identical things, and, actually the significant difference in one analysis of the condition of the feet lay only in 17 patients who waded a stream or who got their feet wet from external sources. Outside of that difference all the rest showed the same pattern of wetness from external water or from sweat, or dryness of the feet, in controls as well as in frost bite patients. You still have to explain why some people do become frostbitten and others do not, in identical circumstances.

Meryman I should say that is because the controls were not identical to the frostbite cases.

Schuman In what *ways* weren't they? That is what we are trying to elicit here, and that is the purpose of all this analysis For example in Table X one sees a significant difference between patients and controls with respect to history of previous cold injury and in Table XI the patients were less active in identical situations.

TABLE X

Comparison of 664 Cases of Frostbite and 447 Bunker-Mat Controls with Respect to History of Previous Cold Injury Korea 1951-52

History of Previous Cold Injury	Cases		Controls	
	No.	%	No.	%
None	535	80.6	397	88.8
Frostbite	125	18.8	38	8.5
Trench foot	1	0.2	2	0.4
Chilblains	3	0.5	10	2.2
Total	664	100.1	447	99.9

$X^2 = 29.5443$ df=3 $P<.001$

TABLE XI

Comparison Between 700 Cases of Frostbite and 455 Controls with Respect to Intensity of Activity at Time of Exposure, Korea 1951-52

Intensity of Activity	Cases	Controls	Totals
Light	509	251	760
Heavy	191	204	395
Total	700	455	1155
$X^2 = 87.7405$ $P < .001$			

These are the differences being sought and in the race comparison, these differences are not, on the other hand, present.

Adams Ray You have no instance where you had many, say half a company for example, who were all frostbitten and where you could see the difference between the two groups?

Schuman No the weather was not so severe in the 1951-52 experience. However there was one squad, a group of Colombians, who crossed a stream, and went through the ice. But only half of them, that is, about 4 or 5, became frostbitten, and the other half did not. But, again, in a group of nine, chance alone could play a role. The other instance involved some Thailanders. They again, had extenuating circumstances such as you mentioned. They had about 36 cases in a long trek, and yet many times that number were actually exposed to identical circumstances in that convoy of replacements between Vijongbu and their particular front-line positions, when they were hit by a snow storm and their trucks broke down. These boys had never been in temperatures below 57° F I think it was, in Siam. Even their experience with cold weather gear was minimal for it was difficult to teach them to lace their boots. They didn t even know what laces were for They were given gloves, for instance, and told that they would protect them, so they stood there, immobile, on the back of the trucks waiting for the trucks to be repaired, without even moving their fingers. That was the sort of situation you had. But why even among that group and I direct the question to you, Harold, were so many not frostbitten and others frostbitten under the same circumstances, with the same gear etc.?

Meryman Maybe some of them did wiggle their fingers.

Schuman But there are examples of many people in identical circumstances, with identical gear not becoming frostbitten, and the question still remains, why?

Burch May I take issue with the term, identical"? That is a very difficult statement to support. I remember when we first started our studies of peripheral blood vessels almost twenty years ago we were using one finger as a control against another finger on the same subject, studied in an air-conditioned room. We noted im mediately that one finger behaved differently from the other finger A draft from the air-conditioning duct across the ceiling of the room deflected against the wall and hit one side of the subject, while his body shielded the other hand and finger Thus the fingers, though both were in an air-conditioned room, were not really in the same environment. With elimination of the draft the two fingers behaved alike.

Schuman I would grant you a misuse of the term.

Adams Ray Another factor which is very difficult to evaluate is the factor of fear That would give you vasoconstriction and hyperhidrosis.

Schuman Again, that is an innate characteristic or variable.

Webster Don't you think that your experience parallels in some way the experimental work with animals, unless you use extreme temperatures? You get most peculiar variations in the same groups of animals and even in the same animal, where one leg will exhibit much more damage.

Shumacker What was the difference in the incidence of frost bite? Was there as great a difference between southern and northern whites as between Negroes and whites?

Schuman The southern white was 1 6 times as apt to be at tacked as the northern white. The northern Negro had an attack rate of 7 times, and the southern Negro had an attack rate of about 5 times the rate of the northern white. The difference between the northern and southern Negro is not significant. But the point to be noted is the marked difference in attack, irrespective of region, between the two races.

Shumacker I am sure everyone of us hopes that some day you, or someone else, will settle the question of the fundamental factors involved in this obvious difference in incidence of frostbite in Negroes and whites. Even if we fail now and in the future to elucidate this problem, nevertheless it is extremely important that you ha e shown that this striking difference existed in troops operat

ing as mixed Negro-white units down to even squad level. This should be of tremendous value. After all, cold injuries are primarily a military problem and a practical contribution of this sort is most valuable even if we fail to understand the basic mechanisms.

Blair: Yes, I think that is a very good point, Dr Shumacker. For example, during one winter of World War I the French used Senegalese troops. Among the Senegalese there were many cases of trench foot whereas none occurred among the white French soldiers serving with them.

For the first time, Commander Schuman has definitely pointed out, statistically that which many of us have suspected for some time. That, I think, is in itself a most valuable contribution to the Armed Forces for selection and assignment of personnel in any type of cold-weather operation.

Schuman: Colonel Orr and Captain Fainer in 1950-51, in a general way indicated a trend in their observation of the state of origin of the individual, that is, where he lived the greatest part of his life and his rate of attack in cold injury. In the 1951-52 data, a very careful analysis was made. We used the United States Department of Commerce data on average minimum January temperatures for the individual states. In some instances, observations that have covered a period of 76 years, and in others for the last 20 or 30 years, were represented. We found that these weather determinations were representative for the state because the stations are, in almost every instance, aggregated where the greatest bulk of the population live. We felt therefore, that because we were using broad, general groups of ten degrees between regions, it made no difference whether there was a five-degree difference in northern Idaho as compared with southern Idaho.

With that in mind, the states were then broken down (Figure 10) on the basis of less than 10° F as the mean of daily minimum January temperatures for the given states in Region I, Region II those states in which the average or mean daily minimum January temperatures ranged from 10° to 20° F., Region III from 20° to 35° F Region IV over 35° F. A fifth region, to include Hawaii, from which there were one or two individuals and Puerto Rico, from which there were about 30 individuals, was added to Region IV because the temperatures obviously were over the 35° F range.

Siple: Very possibly of greater significance than the temperature alone is the length of time that specific temperatures persist. There are some maps in existence which I believe have not been published but could be made available to you that give the per cent of hours

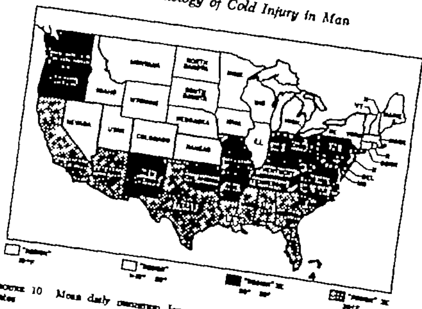


FIGURE 10 Mean daily minimum January temperatures (°F) for the individual states

of the year when the temperature occurs at different degrees for all different intensities. They won t vary very greatly in that, but they might rectify in a given state, in one direction or another

Schuman That is interesting and I would like to have such data to make a test of the particular dichotomy that we used here. We made the split between Region II and Region III, so that Regions I and II represented the North and the rest of the regions, the South.

When the chi-square test was applied to the distribution of our data according to region (Table XII) Region III showed no significant differences between the cases, the epidemiological controls and the pre-exposure controls and could be considered the pivot region. The cases were compared separately with both control groups because of the possible objection that our epidemiological controls might not have represented a cross section of the troops in the Eighth Army across the lines. The pre-exposure controls which represented a study of 1,359 individuals across the entire front, are more nearly representative of the entire population. We then find that there are highly significant differences. In the analysis of the individual chi-square cells we found a surplus of cases coming from the southern regions The expected frequency is given by the first asterisk for the epidemiological controls or the

TABLE XII

Comparison of 701 Cases of Frostbite, 452 Epidemiologic Controls and 1359 Pre-Exposure Controls with Respect to Climatologic Region of Origin, Korea 1951-52

Region	Cases		Epidemiologic Controls		Pre-Exposure Controls	
	No.	%	No.	%	No.	%
I	22	3.1	39	8.6	121	8.9
II	115	16.4	117	25.9	329	24.2
III	281	40.1	148	32.7	604	44.4
IV	228	32.5	100	22.1	275	20.2
V	55	7.8	48	10.6	30	2.2
Total	701	99.9	452	99.9	1359	99.9
χ^2	—		44.6525		101.4641	
P	—		<.001		<.001	
North (I II)	137	19.5	156	34.5	450	33.1
South (III, IV V)	564 (523) (501)†	80.5	296	65.5	909	66.9
χ^2	—		82.4900		41.7692	
P	—		<.001		<.001	

Expected on basis of Epidemiologic Controls
† Expected on basis of Pre-Exposure Controls

bunker mate controls, and the expected frequency on the basis of the pre-exposure controls is represented by the dagger Each of them is significant. I took Colonel Orr's data of 1950-51 and compared it with my data. I found that the same distribution and the same preponderance of cases from the southern states existed in the preceding year's experience, which I tested and found to be statistically significant.

Shumacker. Commander Shuman, have you made this same sort of table excluding the Negroes?

TABLE XIII

Comparison of 408 White Cases of Frostbite and 404 White Epidemiologic Controls with Respect to Region of Origin, Korea 1951-52

Region of Origin	White Cases	White Epidemiologic Controls	Total
Northern	113	154	267
Southern	295 (273)	250	545
Total	408	404	812
$X^2 = 9.9920$ $P < .01$			

Schuman. Yes, we have the following to go on. In Table XIII we separated the cases among whites from those among Negroes and, utilizing the state of origin or region of origin as I and II for the North and III, IV and V for the South, we again found an excess of cases among whites in the South over the expected for a chi-square of 9.992, and the probability of occurrence by chance less than one in 100. Again, because we used the bunker mate or

TABLE XIV

Comparison of 408 White Cases of Frostbite and 1146 White Pre-Exposure Controls with Respect to Region of Origin, Korea 1951-52

Region of Origin	White Cases	White Pre-Exposure Controls	Total
Northern	113	437	550
Southern	295 (264)	709	1004
Total	408	1146	1554
$X^2 = 14.8323$ $P < .001$			

epidemiological controls and anticipated criticism that this was not representative of the front as a whole, we did the same thing with the pre-exposure controls (Table XIV) which were similar to the population of the Eighth Army as a whole, and obtained an even greater number in the South than was expected.

Kark What is the general distribution of soldiers in the whole Army? How many in the Army come from the North as compared to the South?

Schuman That, of course, as you know is automatically taken care of in a chi-square on the basis of expectancy for these tables. The bulk of the people come from the South. You can expect 264 cases as compared to 113 in the North. It doesn't seem very startling, but by actual proportion you find that there is a highly significant difference between the two, and that that could occur by chance alone less than once in 1000 I did not actually calculate the total probability value there.

Brinkhous I wonder if that difference may not be related to the AGCT tests and educational background. With comparatively limited educational opportunities in many sections of the South, a greater proportion of the boys there are likely to be channeled into the rifleman group

Siple More industrial deferment, perhaps?

Schuman Your point, of course, refers to why so many more boys from the South get into the Army and your observation, Dr Brinkhous is a matter of explaining this particular difference I do not have the answer I am only reiterating that these regions have

TABLE XV

Comparison of 286 Negro Cases of Frostbite and 37 Negro Epidemiologic Controls with Respect to Region of Origin, Korea 1951-52

Region of Origin	Negro Cases	Negro Epidemiologic Controls	Total
Northern	24	1	25
Southern	262 (264)	36	298
Total	286	37	323
$\chi^2 = 1.4848$ $P > .20$			

been classified on the basis of temperature and not as political subdivisions usually referred to as North and South.

Shumacker Didn't you separate these two groups on the basis of AGCT scores?

Schuman Yes, I shall discuss that later. We made the same regional comparisons for cases among Negroes (Table XV). I was very unhappy about having only 37 bunker-mate controls and obtained a probability of greater than .2 or 20 per cent with the Yates correction for continuity. In utilizing the pre-exposure controls for the Negroes as well (Table XVI) we had a few more

TABLE XVI

Comparison of 286 Negro Cases of Frostbite and 196 Negro Pre-Exposure Controls with Respect to Region of Origin, Korea 1951-52

Region of Origin	Negro Cases	Negro Pre-Exposure Controls	Total
Northern	24	12	36
Southern	262 (265)	184	446
Total	286	196	482
	$X^2 = 0.8063$	$P > .30$	

from the North and a lot more from the South. We expected 265 and got 262, so that I can conclude from this particular experience that as far as the Negroes are concerned, the region of origin, North versus South, does not seem to play a part in contributing to the excess of cases among Negroes. Thus, from these two groups of data, I would say that whatever it is that is operating in race, race is the predominant factor and climatic region is secondary in this particular experience.

Then we compared the white cases with the Negro cases (Table XVII) which, in a sense, is almost a duplication merely to draw out differences in the South, and did find that the southern Negroes had a significant preponderance over expectancy corroborating that race and all that goes with race has a more prominent role in this picture.

TABLE XVII

Comparison of 408 White Cases and 286 Negro Cases of Frostbite with Respect to Region of Origin, Korea 1951-52

Region of Origin	White Cases	Negro Cases	Total
Northern	113	24	137
Southern	295	262 (229)	557
Total	408	286	694
$X^2=39.5481$ P< 001			

TABLE XVIII

Comparison of 702 Cases of Frostbite and 448 "Bunker-Mate" Controls with Respect to Type of Residence Lived in for Greater Part of Life, Korea 1951-52

Type of Residence	Cases		Controls	
	No.	%	No.	%
Rural	158	22.5	106	23.7
Urban and Suburban	544	77.5	342	76.3
Total	702	100 0	448	100.0
$X^2=0.2057$ P>.50				

Table XVIII indicates that we found no significant difference in the distribution of cases by type of residence. I deliberately combined suburban with urban, primarily because of the disparity in questioning between the patients and the controls. Actually suburban referred to towns on the outskirts of large cities or contiguous with large cities This was an attempt to elicit the existence of a difference in attack rate among people who come from strictly rural environments as compared to strictly urban in other words, a man waiting for a bus on a corner can get out of the cold by going into the corner drugstore, but a boy living on a farm has to

go about his chores regardless of how cold it is. This was done again with an eye toward the climatologic factor there.

Siple: With respect to your climatological interpretation, I would like to attack one point. California, for example, has a distinctly different climate from the North or South, in the other areas of the United States. I think that significantly at least it should be examined, because of the fact that our West Coast cities don't have either hot weather or cold weather whereas in the interior and much of the East there are long periods of both extreme cold and extreme heat.

I think there are three specific climates to be considered, and that it is conceivable that your California statistics thrown in with the South, may prove erroneous. At our first conference we referred to the British, who perhaps live at almost the lowest possible level of physiological climatic adjustments. The British seem to be able to get along without central heating in their homes because it never gets so cold that they can't get by with more simple heating systems. This creates a specific living pattern and must affect the whole physiological adjustment of the British to the cold. This same situatiton is similarly true of our West Coast cities. There are some important differences between the north and south of California, however, as a whole there may be a significant pattern in respect to the rest of the country to be watched.

Schuman: I was aware of that particular thing. I excluded the patients who lived in California and excluded those from the controls and it didn't seem to make any difference.

The several factors which may have contributed to the climatic regional differences were tested next (Table XIX). Because race differences had been noted, these were analyzed separately for northern and southern regional differences.

The first significant item on Table XIX is the previous cold injury experienced. Northern whites, as might be expected, showed a greater number of patients with previous cold injury than southern whites, but the northern Negro and the southern Negro showed an almost identical percentage of patients with previous cold injury. However, soldiers from the southern regions had a higher incidence of frostbite which, if previous cold injury were the only factor operating, would not have been expected since the percentage of previous cold injury among the northern controls is greater.

Table XX shows these race-regional differences in expected attack rates on the basis of previous cold injury. Because the northern troops more frequently gave histories of previous cold injuries, the

TABLE XIX

Summary of Analyses of Factors Tested for Regional and Racial Differences in Frostbite, Korea 1951-52

Item	Race and Region				Test of Significance	Value	df	P
	White		Negro					
	N	S	N	S				
Mean Age (Yrs.)	22.0	22.0	22.3	21.6	t	[illegible]	[illegible]	[illegible]
Rank	—	+	—	+	X^2	[illegible]	[illegible]	[illegible]
Days in Korea	—	+	—	+	X^2	[illegible]	[illegible]	[illegible]
Days in Combat	39.2	36.5	34.5	40.1	t	[illegible]	[illegible]	[illegible]
Days in Combat without Rest	11.6	13.8	7.0	9.9	t	[illegible]	[illegible]	[illegible]
Previous Cold Injury	+	—	—	+	X^2	[illegible]	1 1	[illegible]
Previous Illness (Malaria)	—	+	=	=	X^2	[illegible]	[illegible]	[illegible]
Smoking (Packs)	1.0	0.8	1.0	0.7	t	[illegible]	[illegible]	[illegible]
Hours Eaten before Frostbite	7.2	8.7	6.1	9.6	t	[illegible]	[illegible]	[illegible]
Content of Last Meal (Hot Meal)	+	—	—	+	X^2	[illegible]	4 4	[illegible]
Footgear Worn (Adequate)	—	+	—	+	X^2	[illegible]	[illegible]	[illegible]
Extra Footgear Carried	=	=	+	—	X^2	[illegible]	4 4	[illegible]
Average Change of Socks (Days)	1.4	[illegible]	1.7	1.7	t	[illegible]	[illegible]	[illegible]
Average Change of Innersoles (Days)	1.5	1.3	1.4	1.8	t	[illegible]	[illegible]	[illegible]
Sockgear Worn	—	=	—	+	X^2	[illegible]	[illegible]	[illegible]
Last Change of Socks (Days)	1.0	1.1	1.1	1.8	t	[illegible]	[illegible]	[illegible]
Condition of Feet (Dry)	+	—	+	—	X^2	[illegible]	[illegible]	[illegible]
Condition of Hands (Dry)	—	+	+	—	X^2	[illegible]	[illegible]	[illegible]
Activity	—	+	—	+	X^2	[illegible]	[illegible]	[illegible]
Average Min. Temp of Exposure	10.0	12.0	16.5	13.6	t	[illegible]	[illegible]	[illegible]
Duration of Exposure (Hr.)	11.3	10.4			t	0.374	674	> .70
School Grade Completed	11.5	10.2	10.9	9.3	t	[illegible]	[illegible]	[illegible]
AGCT Score Area I	103.5	89.3		73.9	t	1.570	[illegible]	> .10
AGCT Score Area III	104.7	88.5	86.5	73.8	t	[illegible]	[illegible]	[illegible]
Personal Hygiene	+	—	+	—	X^2	[illegible]	[illegible]	[illegible]

TABLE XX

Expected and Actual Incidence of Frostbite Cases with History of Previous Cold Injury by Race and Region, Korea 1951-52

Region and Race	Pre-Exposure Sample			No. of Cases Frost bite	Expected No Cases with Prev Cold Inj.	Actual N Cases with Previous Cold Inj	diff	X^2	$\Sigma(X^2)$
	Previous Cold Inj.	Total	% Previous Cold Inj						
Northern White	93	497	19 1	109	20.8	31	10 2	5 002	
Southern White	71	790	9.0	274	24 7	52	27.3	30.1 4	
White Subtotal	164	1273	12.9	383	49 4	83	33.6	22.853	35.176
Northern Negro	6	25	24 0	21	5.0	3	2.0	1 333	
Southern Negro	28	249	11.2	249	27 9	43	14.1	7.126	
Negro Subtotal	34	274	12.4	270	33.5	45	11.5	3 048	8 459
Grand Total	108	1547	12.8	653	83 6	128	44.4	23.590	43.635

probability of subsequent injury among these would be greater. Adjustment was made for this difference (expected number of cases with previous cold injury) by region and race and comparison made with actual number of cases which occurred. It can be seen that both northern and southern whites had significant excesses but that the excess of southern white cases of frostbite with previous cold injury was markedly greater Chi square tests for interaction with race and region revealed (sum of the individual chi-squares minus chi-square of the total equal 20 055 and, with three degrees of freedom, the probability is less than 001) that previous cold injury did not affect the groups equally Chi-square tests for regional interaction showed that region contributes significantly to this excess. (Sum of the individual chi-squares for whites minus the chi square of the white sub-total equal 12.323 and, with one degree of freedom, the probability is less than 001) Chi square tests for racial inter-action (southern Negro vs. southern white only because the number of cases among northern Negroes was too few for reliability) showed that race did not contribute to the excess (sum of the individual chi-squares for southern whites and southern Negroes minus the chi-square of the southern sub-total equal 0.915 and, with one degree of freedom, the probability is greater than .30)

The next significant difference between regions is in previous illness. Syphilis seemed to play a part in the difference but whether it contributed to cold injury is unknown. Malaria seemed to be predominant in the southern troops, and, of course, the history of malaria is obviously one of southern locale. How much of this is actual malaria, I don t know and hence, undue significance cannot be attached to this item. We have had personal experience in tracking down reported cases of malaria over the past five to seven years and a lot of malaria is still being reported without laboratory confirmation and it gets into the official reports as malaria, but I know having worked among southern people for a number of years in nutrition surveys, that they call any chill or any fever malaria.

Shumacker For that matter even in southern Illinois.

Burch I might throw some light on the incidence of malaria. I have not had a patient, a native of Louisiana, in the Charity Hospital with malaria since 1941.

Schuman It is an indication of how it has declined. The only malaria we have today in Illinois, for example, where we have one or two indigenous cases a year are 50 to 60 imported cases from the Korean theater

Burch That is our experience, too.

Schuman: In practical terms actually there are significant differences in smoking. Northern patients smoked a little bit more than southern patients yet, the southern troops had more cold injury. As indicated in the race differences in the earlier chart, the Negro smoked less. What that means is highly speculative and we may be putting too much credence on 0.2 of a pack difference though it is statistically important. How important this is physiologically I do not know.

There is a significant difference of one and one-half hours in the interval between their last hot meal and their frostbite on the part of the northern white patients and the southern white patients. But, how important is one and one-half hours physiologically? Did the shorter interval mean they were warmer? A marked difference in interval exists for northern and southern Negroes yet, regional differences in incidence for the Negro were not statistically significant. Another significant item, school grades completed, appears. The northern whites complete more grades of school than do the southern whites, whose education many times is more comparable to that of southern and northern Negroes. Those differences are significant between North and South for the white but are not significant between North and South for the Negro. Can this be said to contribute to the higher incidence of cold injury among southern whites and among Negroes as a whole? Does one more year of schooling better enable the individual to cope with living in the cold? The AGCT scores reveal no significant differences for the northern and southern whites or northern and southern Negroes, which is not incompatible with the discussions so far.

That is the evidence of climatologic regional difference that we have been able to gather from this particular study. That there is a significant difference has been tested by statistical means. Just where those differences lie has not been conclusively determined. Is it acclimatization? Does it bear out some of the animal work that has been done? Does it mean that people from the South are not as well acclimated to cold as are people from the North? This is based entirely on a greater period of exposure to northern climates. The question has been raised in our own laboratory as to whether or not it is the last few years of existence before being exposed to severe environmental conditions that are more important.

Blair: I would like to comment on your data, Commander Schuman, because this is the first opportunity I have had to see it since leaving Fort Knox. The data definitely point out, geographically speaking, the importance in the epidemiology of cold injury of

previous environmental background of the North or South. There is no doubt about that.

I have been quite interested in acclimatization to cold, and I do not believe that this geographical difference can be explained on a strict acclimatization basis. We know from animal experimentation that however resistant to cold injury you may make an animal through previous acclimatization to cold, it is only a short period of time, usually about two months before that resistance has completely disappeared. Presumably all these soldiers, from the North or the South, had been together for many months, a period in which any differences in acclimatization due to previous geographic background would have been totally lost. We know very little about cold acclimatization in the human but we do know quite a bit about acclimatization to heat. I believe Dr Horvath would agree that studies at Fort Knox during World War II and at the Harvard University Fatigue Laboratory before that show that acclimatization to heat is completely lost after a month. So, I feel rather confident that any acclimatization to cold these soldiers may have had from their previous geographical background had been lost by the winter of 1951-52 in Korea.

The one point which impresses me is that if there is any difference in resistance to cold in soldiers from the North and from the South, it is due to experience and "know how" gained from living in that environment rather than physiological acclimatization. Also, you would expect "know how" or experience to work to the greatest advantage in those with the greatest intelligence or highest AGCT scores In the whites that AGCT score was significantly higher than in the Negroes, and of about the same degree as their susceptibility to cold injury The northern white shows much less susceptibility to cold than the southern white; whereas between northern and southern Negroes, of lower AGCT rating and lower ability to take advantage of experience, *there is no significant difference*. Thus looking at your data from this viewpoint, plus what we know of acclimatization to cold in animals and acclimatization to heat in humans, I believe your data definitely point out that any differences in resistance to cold injury in soldier groups from various geographical environments must be on an experience basis rather than due to physiological acclimatization.

Kark You are talking about what you can measure. Let us assume that there is such a thing as long term acclimatization. The reason why you won't spot it is because you haven't got any means of measuring it. I know that people who have lived all their early lives

in a warm climate, even after they have spent 10 or 20 years in a cold climate, still hate the winter much more than people who have been reared and lived in that cold climate all their lives

Talbott Is that psychological? I don t know I think there is just as good reason for believing it is psychological as physiological.

Blair Is it due to the fact that these people never have had the experience of enjoying the pleasant life of a warm climate, or is it due to something physiological rather than psychological?

Hegnauer I think there is a little better reason for believing it is psychological rather than physiological, because acclimatization to heat does disappear and you have to reacquire it. Unless all the processes of acclimatization to cold are radically different, assuming there is such a thing, they must pose a somewhat similar pattern, so they should disappear

Horvath After all, I don t think we know anything about people who have lived in the cold all their lives, either We really have never studied any such group All we have studied are people who have been put in the cold periodically for from one to three months, maybe some of them for up to a year or so. But I gather that even some of the good old-fashioned explorers were never sure of acclimatization as such and would feel more sure that it is experience and training. Of course Paul has a better reason to argue that than I have.

Siple I think that those of us who have repeatedly gone into polar regions have a fairly strong feeling that there is some change that takes place. In the Transactions of the First Conference on Cold Injury there was a misprint in the time which I gave for the onset of a noticeable change There is something that happens in the first couple of weeks of exposure that has occurred repeatedly in the experience of polar explorers We called it acclimatization, and I am prepared to admit that a great deal of it is what I call accustomization, changes that take place in learning to use one s clothing and getting used to a new life. There is some decided change in the well being for most of the people after about a two-week exposure to cold starting from a warm or temperate climatic base line.

Burton I think those of us who are interested in acclimatization in the human have to admit that it is now proved that there is a change in the human, produced by his getting accustomed to the cold, which can be called a physiological change I have recently been with Dr L. D Carlson at the University of Washington on the West Coast. It seems to me that he has evidence very definite evi-

dence in humans and Mackworth, working at Fort Churchill, Canada, I think, had previously produced completely convincing evidence that in psychomotor performance there was a difference after men had been accustomed to having their hands in the cold. But whether or not that explains these results is a different matter I don t think we should neglect the fact that it is now pretty certain that people who have spent all their lives in a fairly warm climate can be taken to live for up to a month or so in a cold climate, and show a definite physiological and psychomotor change.

Blair That is quite true, sir but in relation to interpretation of these data I don t believe that plays any part. The critical experiment, of course, would be to take a group which has just come from a cold area and a similar group from a hot area and place both groups under similar conditions of cold stress and combat activity Then you would be able to make a proper evaluation, because you would be quite sure that you were dealing with a cold acclimatized group and with a nonacclimatized group. You cannot take groups that have been together in one environment all the summer and then, when cold weather comes say that those who were born and reared in the South are any more or less acclimatized than the group that was born and reared in the North.

Burch You are using the term in a physiological rather than a psychological sense?

Blair: That s correct, physiological rather than psychological acclimatization.

Crismon This, of course assumes that you can distinguish between the state of acclimatization and the utter failure of the necessary changes (for acclimatization) in an individual who never reaches that state. There may be some that never would acclimatize.

Siple We have one bit of evidence in regard to occupations. Out of a group of 33 men, 3 individuals because of their occupation more than anything else obviously displayed a difference in their state of acclimatization after a year of life in the Antarctic. The cook, the radio operator and the weather man, stayed indoors almost all the time. When they went outside, you could recognize them immediately by their clothing and they were apparently colder and looked more uncomfortable as they walked around, as compared to the other 30 men. In addition there was a further subdivision between the men who were and active as compared to the older and more sedentary [illegible] Our dog drivers, for example, out o[illegible] wore less cl[illegible] seemed to enjoy the cold more t[illegible] eral run of [illegible] en. This is a striking

difference that I have experienced in myself over several expeditions as well as a situation that anyone can easily observe among various groups of men.

Horvath: Isn't that, again, the result of experience? Those men who were in the wireless room or who were in the kitchen were in the same position as the drivers were on their very first day. The men who had been outdoors for a year had lost that initial stage which these men who had not changed their situation whatsoever were just completing.

I am not for or against acclimatization to cold, but frankly I have yet to see any positive evidence that you can acclimatize men to cold (4). I feel that there is some suggested evidence that may show, say, that one man may be able to respond better to cold than another man, but I don't think there is any good evidence of acclimatization of cold. Frankly, I feel that anybody who implies that a minor change in rectal temperature or a minor change in the temperature of an extremity indicates acclimatization of cold is just beating up the wrong track.

Talbott: Dr. Crismon, I think you reacted violently to that statement?

Crismon: Well, there are data in existence which are convincing, at least to me, that acclimatization is a real phenomenon (5,6,7,8). It may not be detected with measurements quite as elementary as those which Dr. Horvath mentioned, but with measurements of the ability to adjust to differences in heat load. In my interpretation of it, peripheral vascular adjustments as well as heat production adjustments are involved. These have to do with complicated changes in total body water, electrolyte metabolism, blood volume, and a host of other factors. Data are being accumulated now and they stand in nice relationship in contrast to the changes that have been demonstrated for acclimatization to heat.

Burton: When I spoke about Lauren Carlson's* results, I was referring to the level of concrete measurement that Dr. Horvath wants. Dr. Carlson's data convince me that he has shown this from skin temperature data on exposure, rectal temperature and heat losses and so on, so that this has now been demonstrated in humans. I think the difficulty in the past has been that in order to get it in humans, you really have to expose them. You have to have them bivouac outside for a couple of weeks at least, and previous experiments have stopped short of doing that very difficult thing, and have exposed people for from five or six hours every

*Carlson, L. D. Personal communication.

day so they don t show anything The previous data of three or four years ago equally well, were quite statistically valid, showing that the psychomotor performance, the tactile discrimination and so on did change in humans Although I was very skeptical, as Dr. Horvath seems to be, of physiological acclimatization in humans, I have now changed my mind and am satisfied.

Horvath May I say that I haven t changed my opinion, primarily because I would like to look back at experiments which have been conducted over two-week periods under essentially similar situations. There has been, I think, just as good evidence to the contrary as there now seems to be on the positive side. I would hesitate to believe that just because one group of experimenters found that it goes this way and another group of experimenters a little later found that it goes another way there has been a significant difference in their approach. I think it goes back to what Dr Fremont-Smith has often said about really repeating another person s experiment. The question is how to interpret the two sets of facts even though, in one case, they may be eight or nine years old and, in another case, just about one-half year or a year old.

Blair I think Dr Burton made the point correctly that the reason why one set of data seems to show one thing and another set of data the opposite lies in the degree of exposure to which the individuals are exposed. In animal experimentation, which has largely been my experience, exposure of animals to the same degree of cold stress to which we have been accustomed to exposing human beings produces no demonstrable effects. But if we expose animals to more severe cold, just short of producing pathological effects, then we produce tremendous acclimatization changes.

Acclimatization of humans to the same degree of cold stress as that for our animals would consist of exposing a nearly nude unanesthetized man to a degree of cold just shy of producing frostbite or lethal hypothermia. Such an exposure would be from 12 to 16 hours daily at an ambient temperature between 0 C. and +5° C. No one has ever dared to expose human subjects to such a severe cold stress.

Dr Carlson (9) has exposed his human subjects to a much more severe degree of cold stress than has been previously attempted. As a result, he has demonstrated very definite evidence of cold-acclimatization in his subjects. Two weeks exposure of animals to extreme cold produces only minimal acclimatization effects, but if this same exposure is continued for two months then the effect

becomes very marked, indeed. I think, therefore, that bringing about acclimatization to cold depends upon the intensity of cold exposure, both as to degree and duration of cold stress.

Burton Dr Horvath, no doubt, is thinking of experiments such as the one done many years ago through World War II, where I think they took 12 men from training in Virginia or somewhere, up to Fort Churchill, and the results showed that only two men showed any changes. But if you ask the people concerned with that, or look through their report carefully you will find those were the two men who were really exposed to cold, whereas the others were not exposed to very much cold. They were the two men who drove trucks.

Blair Yes when our men go out into the cold they put on heavy clothing and this added insulation keeps their bodies quite warm, only their face and extremities become chilled. Actually they are subjected to only a relatively mild degree of cold stress, far less than that to which our animals are subjected in cold acclimatization studies.

Horvath Well, let me just say that exposing a nude man to 60 F which is not very cold does give some sort of cold stress. After a period of a week, living at that temperature, in that environment, you get some evidence of disturbed function, at least in the extremities. But I have yet to see, after a week, any indication on the part of any subject that he is better adapted to the cold, either subjectively or by any objective measurements. I just haven't seen it. It may be that we've got to get down to 5° or 50° F but we are going to produce damage long before we get to zero that is, if you keep them there for a long period of time.

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ASCORBIC ACID AND RESISTANCE TO COLD

LOUIS PAUL DUGAL
Department of Experimental Physiol II
Laval University Medical School
Montreal Quebec

I HAVE BEEN asked to plan my remarks so as to be provocative of discussion Everybody will agree that the title I gave as a subject for this discussion is in itself quite provocative especially when one remembers that people like Glickman and his co-workers (1) and Blair and his co-workers (2) have failed to see any value for any vitamin supplements in humans exposed to cold.

THE EFFECT OF ASCORBIC ACID ON RESISTANCE AND ACCLIMATIZATION TO COLD IN ANIMALS

Our research on ascorbic acid originated as an attempt to find possible differences in the ability of animals to resist or become acclimatized to cold, when they were fed equivitaminic and equicaloric diets, in which only the proportions of proteins, fats, and carbohydrates were varied. In order to ascertain the most satisfactory diet during exposure to cold, the self-selection method of feeding was used, and the results so obtained on a few rats were verified on large groups of animals The criteria for the best diet were survival and growth. The results obtained in the first series of experiments showed that for resistance and acclimatization to cold in rats, the diet rich in fat was decidedly superior to the one rich in carbohydrate when both diets contained the same number of calories based on the quantity consumed (3) Table XXI shows the composition of both diets, each diet constituted on the basis of previous self selection by a few rats in the cold. Figure 11 gives the effects of the two diets on the survival of rats exposed to the cold. One hundred rats each weighing around 200 gm. were used in each group after twenty days of exposure at a temperature of −2 C., 85 per cent survived in the group receiving the high fat diet (Diet A) and 50 per cent in the group receiving the high carbohydrate diet (Diet B)

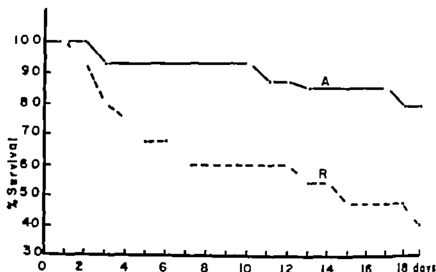


FIGURE 11 The effects of Diets A and R on the survival of rats exposed to cold. Reprinted, by permission, from Dugal, L. P Leblond, C. P., and Thérien, M Resistance to extreme temperatures in connection with different diets. *Canad. J. Res Sect E 23, 244 (1945).*

TABLE XXI

Composition of the Diets Used to Test Resistance and Acclimatization to Cold

Constituent	Diet A (high fat)		Diet R (high carbohydrate)	
	Grams	Calories	Grams	Calories
Casein	4.30	18.9	2.50	11
Glucose	6.20	24.5	20.00	79
Lard	1.86	17.27	0.40	4.65
Yeast	1.25	8	1.25	8
Cod Liver Oil	0.30		0.30	
Wheat Germ Oil	3.71	33.93	0.03	
Mineral Salts	1.00		1.00	
		Total 102.6		Total 102.65

Reprinted, by permission, from Dugal, L. P Leblond, C. P., and Thérien, M Resistance to extreme temperatures in connection with different diets. *Canad. J Res Sect. E 23, 244 (1945).*

In our experiments on small animals like rats and guinea pigs, we considered the transition period from normal temperature to sudden cold, the one during which all animals lose weight, the period of resistance. The criterion for that period was the percentage of survival. The period of acclimatization started when the sur

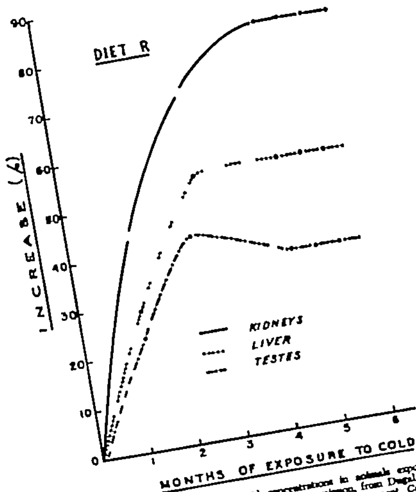


FIGURE 12. The increase in ascorbic acid concentrations in animals exposed to cold and on high carbohydrate diet. Reprinted, by permission, from Dugal, L. P and Thérien, M. Ascorbic acid and acclimatization to cold environment. Canad. J Res. Sect. E 25, 111 (1947).

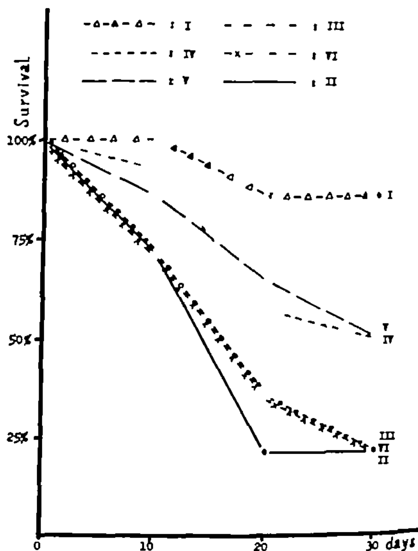


FIGURE 13. The effects of 0.14 mg. per day of adrenalin and/or 150 mg. per day of ascorbic acid on the survival of rats at −1 C. Reprinted, by permission, from Fortier, G., and Dugal, L. P. Adrénaline et résistance au froid. *Rev. canad. de biol.* 11: *185 (1952).*

vivors began to gain weight, and the latter were considered fully acclimatized when they had attained their initial weight at the moment they were first exposed to cold.

Even in the fat fed group the animals that died in the cold all showed the same symptoms of some nutritional deficiency for in-

stance, edema of the penis, swollen legs, necrotic tails, etc. (4) These symptoms can be obtained partially or totally at room temperature in scorbutic or inanitiated animals. Our diets seemed complete except for ascorbic acid which the rat is able to synthesize. But it was possible that exposure to cold might inhibit, in those dying animals, the spontaneous synthesis of ascorbic acid, or better might increase the needs for that vitamin in such a way that these needs could not be met by the endogenous synthesis.

We found in our next series of experiments (Figure 12) that the concentration of ascorbic acid increased gradually and reached a high level in the tissues of rats which succeeded in getting acclimatized to the cold as compared to their controls, kept at room temperature (5). The increase mentioned which was on a wet weight basis was much smaller if the rats exposed to cold were injected daily with ascorbic acid. Rats which died in the cold room had a very low content of ascorbic acid. Caloric intake increased from 70 calories per rat per day at room temperature, to 110 on the average, in the cold room. A few experiments on a limited number of animals (6,7) showed that ascorbic acid did increase the resistance of rats to cold, as measured by the percentage of survival. This finding was confirmed by Mayer (8) and Leblanc *et al.* (9)

TABLE XXII

The Influence of Ascorbic Acid on Survival During Exposure to Cold

7 days exposure to a temperature of —3 C	Number of animals	Number of dead	Survival
Group receiving 150 mg. per day of ascorbic acid	12	3	75%
Controls receiving sodium chloride	12	1	0%

14 days exposure to a temperature of 4 C	Number of animals	Number of dead	Survival
Group receiving 35 mg. per day of ascorbic acid	35	7	80.0%
Group receiving tap water	35	17	51.4%

Reprinted, by permission, from Dugal, L. P. and Thérien, M. The influence of ascorbic acid on the adrenal weight during exposure to cold. Endocrinology 44, 420 (1949)

Figure 13 shows the effects of adrenalin (0 14 mg. per day) and ascorbic acid (150 mg per day) on the survival of rats at –1 C. Group I (the ascorbic acid treated) had 85 per cent survival, Group II (adrenalin treated) Group III (adrenalin combined with ascorbic acid) and group IV (untreated controls) each had a survival of less than 25 per cent, Group IV (sodium chloride treated) and Group V (adrenalin per os) each had 50 per cent survival.

There were 12 rats, each weighing 200 gm., in each group represented in Table XXII. After seven days exposure at –3 C. only 5 of those receiving 150 mg. of ascorbic acid daily died and all 12 receiving sodium chloride died. In the group with longer exposure at 4 C. seven of the 35 animals which received 25 mg. per day of ascorbic acid by mouth died at the end of the 244 days. This is about the same incidence as at room temperature. Seventeen of

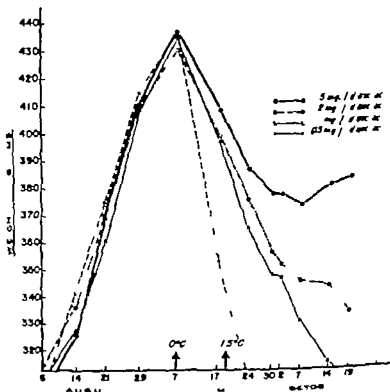


FIGURE 14. The effects of various concentrations of ascorbic acid on acclimatization of guinea pigs to cold as judged by changes in weight. Reprinted, by permission, from Dugal, L. P., and Thérien, M.: Ascorbic acid and acclimatization to cold environment. *Canad. J. Res., Sect. E 25, 111 (1947).*

the 85 in the control group which received only tap water died after 244 days at 4 C.

But, we were, of course, more interested in seeing what would be the effects of vitamin C on the resistance to cold of guinea pigs and monkeys, and that is why we concentrated our efforts on those two species.

More than one thousand guinea pigs were tested, and it was found that those animals needed more and more ascorbic acid as the temperature was being lowered (5) Figure 14 shows that only the group receiving 5 mg. per day of ascorbic acid succeeded in getting acclimatized at a temperature of –1.5 C. The average weight of the guinea pigs, upon entrance into the cold room was 440 grams.

As a matter of fact, many different dosages of vitamin C ranging from 0.5 mg. to 75 mg per day were investigated, most of them by oral administration. The administration of ascorbic acid always started at least three weeks before any group was exposed to cold. Some of those experiments are summarized in Table XXIII. In experiment 3002 the treatment with vitamin C lasted five months, but the duration of exposure to cold was four months during which time the temperature of exposure was gradually decreased from 8° C to –8° C. One group which received 75 mg. per day of vitamin C lost weight at first but returned to the normal or initial weight at the end, the group receiving 25 mg. daily of ascorbic acid exposed for the same time at the same temperature, lost 20 per cent in weight, on the average, whereas, the group receiving 2 mg. per day of the same substance lost 31 per cent in weight, on the average.

In another experiment (3005) with temperatures ranging from 1 C. to 4 C. we compared the effects of 10 5 and 0.5 mg. of ascorbic acid, the group receiving only 0 5 mg. of that substance could not survive at that temperature for more than 16 days, and the animals of that group had, on the a erage, lost 40 per cent of their weight. The group receiving 10 mg. had gained 8 per cent while the weight of those receiving 5 mg had not changed appreciably

It was also found that there i a greater retention of ascorbic acid in the tissues, especially the adrenals, at colder than room temperature this is clear from tissue analysis (Table XXIV) and from urinalysis (10) (Figure 15) In guinea pigs, there is an increase in ascorbic acid excretion during the first days of exposure to cold and then a decrease below the level found at room temperat re

TABLE XXIII

Expt. No.	Amount of asc. acid received daily mg.	Duration of treatment with asc. acid	Duration of exposure to cold	Temperature of exposure degrees C.	Gain in weight during exposure to cold	Average ascorbic content mg./gm.		
						Liver	Kidneys	Adrenals
3002	75.0	5 months	4 months	+8. to −6	− 0.4%	0.113	0.052	0.750
	25.0				−19.6%	0.139	0.046	0.395
	2.0				−31.3%	0.014	0.022	0.072
3005	10.0	4 months	3 months	+1 to −4.	+ 8.3%	0.132	0.052	0.552
	5.0				+ 0.8%	0.063	0.030	0.309
	0.5	1½ months	16 days	+ 1	−40.0%	0.051	0.025	0.036
3011	7.5	3 months	2 months	+1 to −2.5	+ 7.0%	0.084	0.040	0.437
	2.5				+ 2.6%	0.059	0.027	0.272
3016	5.0	2½ months	1½ months	0 to −1.5	−12.0%	0.066	0.033	0.221
	2.0				−22.5%	0.063	0.025	0.133
	1.0				−29.1%	0.055	0.022	0.126
	0.5	1½ months	17 days	0.	−40.0%	0.030	0.024	0.035
3030	10.0	2 months	1 month	−1.5 to −2.0	− 8.3%	0.099	0.009	0.047
	2.0				−13.0%	0.063	0.084	0.318

Reprinted, by permission, from Dugal, L. P. and Thérien, M. Ascorbic acid and acclimatization to cold environment. Canad. J. Res., Sec. E, 25, 111 (1947).

the excretion remains at a low level during the whole period of exposure to cold and even for a while when the animals are brought back to room temperature.

As in the rat, failure of acclimatization to cold is accompanied by a decrease in the ascorbic acid content of the adrenals. The average ascorbic acid concentration in the adrenals of guinea pigs dying

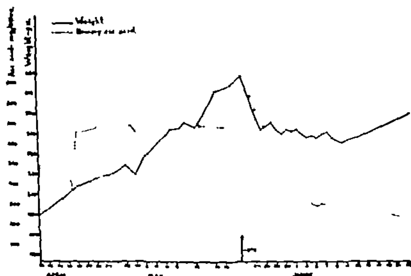


FIGURE 15. Excretion of ascorbic acid by guinea pigs before and after exposure to cold. Reprinted, by permission, from Thérien, M., and Dugal, L. P. Excrétion urinaire d'acide ascorbique chez les rats et les cobayes exposés au froid. *Rev. canad. de biol.* 8, 249 (1949).

TABLE XXIV

Retention of Ascorbic Acid by Guinea Pigs Exposed to Cold

Ascorbic acid given daily mg.	Days of exposure to cold	Average weight during exposure gm.		Temperature of exposure degrees C.	Average ascorbic acid content, mg./gm.		
		Initial	Final		Liver	Kidneys	Adrenals
10	15	438.1	570.5	0	0.008	0.041	0.550
10	0	420.4	495.0	20	0.065	0.035	0.369

Reprinted, by permission, from Dugal, L. P. and Thérien, M. Ascorbic acid and acclimatization to cold environment. *Canad. J. Res. Sect. E* 25, 111 (1947).

TABLE XXIII

Expt. No.	Amount of asc. acid received daily mg	Duration of treatment with asc. acid	Duration of exposure to cold	Temperature of exposure degrees C.	Gain in weight during exposure to cold	Average ascorbic content mg./gm.		
						Liver	Kidneys	Adrenals
3002	75.0	5 months	4 months	+8. to −6.	− 0.4%	0.113	0.052	0.750
	25.0				−19.6%	0.139	0.046	0.395
	2.0				−31.3%	0.044	0.022	0.072
3005	10.0	4 months	3 months	+1 to −4.	+ 8.3%	0.132	0.052	0.552
	5.0				+ 0.8%	0.063	0.030	0.309
	0.5	1½ months	16 days	+ 1	−40.0%	0.051	0.025	0.036
3011	7.5	3 months	2 months	+1. to −2.5	+ 7.0%	0.094	0.040	0.437
	2.5				+ 2.6%	0.059	0.027	0.272
3016	5.0	2½ months	1½ months	0 to −1.5	−12.0%	0.066	0.033	0.221
	2.0				−22.5%	0.063	0.025	0.133
	1.0				−29.1%	0.055	0.022	0.126
	0.5	1½ months	17 days	0	−40.0%	0.030	0.024	0.035
3030	10.0	2 months	1 month	−1.5 to −2.0	− 8.3%	0.080	0.039	0.647
	2.0				−13.0%	0.063	0.024	0.316

Reprinted, by permission, from Dugal, L. P. and Thérien, M. Ascorbic acid and [illegible] acclimatization to cold environment. Canad. J. Res. Sect. E 25, [illegible] 1 (1947).

the excretion remains at a low level during the whole period of exposure to cold and even for a while when the animals are brought back to room temperature.

As in the rat, failure of acclimatization to cold is accompanied by a decrease in the ascorbic acid content of the adrenals. The average ascorbic acid concentration in the adrenals of guinea pigs dying

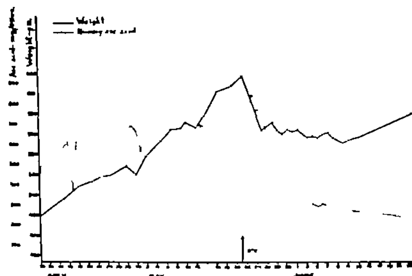


FIGURE 15. Excretion of ascorbic acid by guinea pigs before and after exposure to cold. Reprinted, by permission, from Thérien, M., and Dugal, L. P. Excrétion urinaire d'acide ascorbique chez les rats et les cobayes exposés au froid. *Rev. canad. de biol.* 8, 243 (1949).

TABLE XXIV

Retention of Ascorbic Acid by Guinea Pigs Exposed to Cold

Ascorbic acid given daily mg.	Days of exposure to cold	Average weight during exposure, gm.		Temperature of exposure degrees C.	Average ascorbic acid content, mg./gm.		
		Initial	Final		Liver	Kidney	Adrenals
10	15	436.1	378.5	0	0.096	0.041	0.550
10	0	420.4	493.0	20	0.065	0.035	0.869

Reprinted, by permission, from Dugal, L. P. and Thérien, M. Ascorbic acid and acclimatization to cold environment. *Canad. J. Res. Sect. E* 25, 111 (1947).

in the cold room has been compared (Table XXV) with the expected average concentration in the adrenals for different dosages, and a decrease of 60 per cent in the ascorbic acid concentration of the adrenals has been found for those animals which died. It must be emphasized that it is in the adrenals that the decrease is most pronounced.

TABLE XXV

Average Ascorbic Acid Concentration in the *Adrenal Glands of Guinea Pigs Dying in the Cold Room*

Ascorbic acid given daily mg.	Rectal temperature degrees C.	Adrenal asc. acid, mg/gm	
		Expected	Found
2.0	25	0.228	0.063
2.0	25	0.228	0.054
2.0	23	0.228	0.058
2.0	20	0.228	0.031
2.0	20	0.228	0.053
0.5	28	0.175	0.016
5.0	30	0.399	0.249
5.0	18	0.399	0.215
5.0	19	0.399	0.208
7.5	15	0.532	0.438
10.0	21	0.710	0.105
Average		0.343	0.138 (−60%)

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In order to find out if ascorbic acid had the same beneficial effects on larger mammals a series of experiments with Rhesus macacus monkeys was undertaken. Twenty four monkeys were distributed into three groups; Group I, the control group, consisting of 11 monkeys was kept constantly at room temperature and fed Purina Dog Chow plus an oral supplement of 25 mg. of ascorbic acid daily for six months. Group II consisting of 8 monkeys, was given an identical diet and the same amount of ascorbic acid as

the preceding group but was maintained in a mildly cold environment of 10 C. for six months before any experiment was performed on it, and finally the 5 monkeys of Group III were also kept at the same mildly cold temperature for six months and fed the same diet as Groups I and II but received daily 325 mg. of ascorbic acid orally Acclimatization to cold was estimated by comparing the respective capacities of Groups II and III to resist an acute exposure of two hours at −20 C. with the resistance of the control group In all these experiments, the monkeys were completely at rest and immobilized during the whole exposure. The degree of resistance to that intense cold, was measured by the ability of the different groups to maintain their rectal and intramuscular temperatures during exposure. The incidence of frostbite of the tails in all those monkeys was analyzed.

The monkeys were immobilized in wooden boxes, their fingers and toes covered with mittens to prevent frostbite but their tails were uncovered as shown in Figure 16. One thermocouple was inserted in the rectum and the other one (needle type) in the right thigh. Both were plugged into a connecting box in which eight additional thermocouples could be inserted. Never more than three monkeys were exposed at the same time. A push-button system connected any electrode with a compensated galvanometer always kept at room temperature giving direct readings to a tenth of a degree centigrade within a few seconds. The temperature of the cold room, the differential of which was 1.5° C. was constantly given by a recording thermometer The relative humidity was constant at 60 per cent.

Table XXVI presents the results obtained in the three groups of monkeys (11) The animals of Group I had been exposed sixty two times at −20 C. but never more than once a week. When they had frostbite, we waited until they were completely cured before exposing them again. The fall in rectal temperature for this group is 3 C. Group II pre-exposed at 10 which had grown much thicker fur had exactly the same fall in rectal temperature. But Group III pre-exposed at the same mild cold temperature and receiving 325 mg. of ascorbic acid daily had a fall in rectal temperature of only 2.1 C. a difference of 0.9 C. which is statistically very significant. (The t test is 5.41 between groups I and III, and 4.74 between groups II and III) We get about the same picture when we look at the results obtained on intramuscular temperature Group I which had never been exposed to cold had a fall of 4.7 C. in intramuscular temperature when exposed to −20 C. Group II

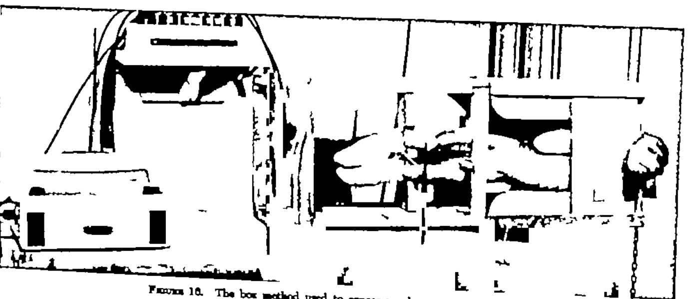


FIGURE 16. The box method used to expose monkeys to extreme cold.

TABLE XXVI

Changes in Rectal and Intramuscular Temperatures of Monkeys Exposed to Cold

Group	kg.	Ascorbic acid mg/day	Acclimatized at C	No. of exposures at −20 C.	Fall in rectal temp C.	% Diff. between	t	Fall in intramuscular temp., C.	% Diff. between	t
I	5.4	25	20	62	3.07 ± 0.12	I & II 2.3	0.87	4.70 ± 0.28	I & II 6.9	0.71
II	5.6	25	10	49	3.00 ± 0.15	I & III 31.5	5.41	5.05 ± 0.41	I & III 23.0	2.60
III	5.7	325	10	81	2.10 ± 0.12	II & III 30.0	4.74	3.62 ± 0.31	II & III 28.3	2.78

Reprinted, by permission, from Dugal, L. P. and Fortier, G. Ascorbic acid and acclimatization to cold in monkeys. *J. Appl. Physiol.* 5, 143 (1952).

TABLE XXVII

Average Fall of Rectal Temperatures Following Exposures to —20 C° for Five Monkeys Receiving Varied Amounts of Ascorbic Acid

Subjects No.	1	2	4	5	6	Averages
25 mg. asc. acid daily	−2.66 (6)	−2.66 (7)	−3.78 (9)	−2.90 (6)	−2.70 (3)	−3.04 ± 0.18
325 mg. asc. acid daily	−1.57 (8)	−2.18 (6)	−2.32 (5)	−1.85 (4)	−2.60 (7)	−2.10 ± 0.12
Diff. in degrees C.	1.09	0.48	1.46	1.05	0.10	0.94 (t=4.29)

The figures in parentheses represent number of exposures.

TABLE XXVIII

A erage F ll in Intramuscular Temperatures Following Exposures to —20° C for the Same Monkeys as Shown in Table XXVII

Subjects No	1	2	4	5	8	Average
25 mg. asc. acid daily	3"3 (6)	—9 4 (7)	—4 02 (6)	—5.42 (6)	—6 27 (3)	—5 "3 ± 0.56
125 mg. asc. acid daily	—3 15 (8)	—6 3" (6)	—. 12 (5)	—3 67 (3)	—2.87 (7)	—3 62 ± 0.3.
Diff n degrees C.	0 55	3.3"	1 90	1.75	3.40	2.13 (t=3 34)

The figures in parenthesis represent number of exposures

had a fall which is a little higher but the difference between the two is not significant. Group III had a fall of only 3.6° C. Here again, the difference between Group III and Groups I and II is significant.

Different treatments on the same animals were compared (Table XXVII) Monkey No. 1 was exposed to 10 C. for six months and received 325 mg. daily of ascorbic acid orally He was then exposed eight times, each time for two hours at −20 C. with never more than one exposure a week. The average fall of his rectal temperature was 1.57 C. For the next three months this monkey was maintained at 10 C. and received only 25 mg of ascorbic acid. In the following six months, he was exposed six times to −20° C. and his average rectal temperature fall was 2.66 C.

Monkey No 4 had a fall in rectal temperature of 3.78 C. when receiving 25 mg. of ascorbic acid and only 2.32 C. when receiving 325 mg. Monkey No 5 had a fall of 2.90 C. and 1.85° C., respectively in the same conditions. Monkeys No 2 and 8 received 25 mg. of ascorbic acid when they were first pre-exposed to cold and in the following year they received 325 mg. with falls in rectal temperatures of 2.18 C. and 2.66 C., and 2.60 C. and 2.70 C., respectively This order was designed to eliminate an association between the result and the order of exposure

The average fall (weighted average) in rectal temperature was 3.04 C. when the monkeys received 25 mg. of ascorbic acid and 2.10 C. when the same monkeys received 325 mg. of ascorbic acid.

Table XXVIII shows the fall in intramuscular temperatures for the same monkeys, during the same experiment. The average difference although quite high and less significant than for rectal temperatures is still highly significant The t test is 3.3, but the individual variability for intramuscular temperatures is much more pronounced than it is for rectal temperatures.

Table XXIX shows the effect of daily administration of 325 mg. of ascorbic acid for at least one month before exposure on the tolerance to intense cold of monkeys which had never previously been exposed to cold. Each group consisted of six monkeys. The average fall in rectal temperature of the group receiving 25 mg. of ascorbic acid is 3 1 C. and almost 2.5 C., in the group receiving 325 mg The difference obtained here is much smaller than it was with monkeys pre-exposed to cold but it is still significant.

TABLE XXIX

The Effect of Various Dosages of Ascorbic Acid on the Tolerance to Intense Cold of Monkeys not Pre-exposed to Cold as Shown by Rectal Temperatures

Group	Number of subjects	Average weight, pounds	Number of experiments	Average fall (° C) in rectal temperature	% diff and t value
I. Normal temp, ascorbic acid 25 mg. daily	6	14 0	21	3 14 ± 0 17	27 1%
II. Normal temp ascorbic acid 325 mg. daily	6	13.8	19	2.47 ± 0.13	3.14

TABLE XXX

The Effect of Various Dosages of Ascorbic Acid on the Tolerance to Intense Cold of Monkeys not Pre-exposed to Cold as Shown by Intramuscular Temperatures

Group	Number of subjects	Average weight, pounds	Number of experiments	Average fall (° C) in intramuscular temperature	% diff and t value
I. Normal temp. ascorbic acid 25 mg. daily	6	14 0	21	5 79 ± 0 33	19 1%
II. Normal temp. ascorbic acid 325 mg. daily	6	13 8	18	4 88 ± 0.43	1.61

The intramuscular temperature difference (Table XXX) is very slight, and it is not significant (12) The results indicate that it is the combination of pre-exposure to cold plus large amounts of ascorbic acid that favors the acclimatization and the resistance to intense cold in the monkey

On the left in Table XXXI are the data concerning the monkeys not pre-exposed to cold and receiving _3 or 3_3 mg of ascorbic acid daily and on the right are the ones concerning the animals pre-exposed to cold and receiving _5 and 3_5 mg respectively

TABLE XXXI

The Frequency of Frostbite After Exposure for Two Hours at —20 C as Shown in Rhesus Monkeys

Monkey	Not pre-exposed to cold				Pre-exposed to cold			
	25 mg./day of ascorbic acid		325 mg./day of ascorbic acid		25 mg./day of ascorbic acid		325 mg./day of ascorbic acid	
	Number of exposures	Exposures with frostbite	Number of exposures	Exposures with frostbite	Number of exposures	Exposures with frostbite	Number of exposures	Exposures with frostbite
1					6	2	7	0
2					8	2	6	0
4					9	8	5	0
5					6	1	4	0
8					3	0	6	1
9	7	2	4	0				
10	4	2			6	0		
12	3	0			7	3		
13	6	3			5	3		
14	12	3						
18	4	2	1	0				
20			5	1				
22			4	4				
23	4	4						
Total	40	16	14	5	48	17	28	1
%	40%		35.7%		35.4%		3.6%	

When monkey No 1 which received 25 mg. of ascorbic acid was exposed six times to −20 C., twice he had a stiff tail when he came out of the cold chamber and developed gangrene. But when he received 325 mg. of ascorbic acid, this same monkey never had any frostbite This was true for monkeys Nos. 2, 4, 5. Only No 8 is an exception.

If we take the average of 40 exposures in the group not pre-exposed to cold and receiving 25 milligrams of ascorbic acid, we have 16 cases of frostbite or 40 per cent. Among the animals not pre-exposed to cold and receiving 325 mg. of ascorbic acid there were 5 cases in 14 exposures or 35 per cent. When there were 48 exposures in animals pre-exposed to cold for at least six months and receiving 25 mg. of ascorbic acid, there were 17 cases of frostbite or 35 per cent. When the animals were pre-exposed to cold and received 325 mg. of ascorbic acid there was only one case of frostbite in 28 exposures or less than 4 per cent.

It has been shown that pre-exposure to cold does increase resistance to cold in animals that are able to synthesize ascorbic acid such as rats and rabbits. Guinea pigs and monkeys are unable to synthesize ascorbic acid and it is not known whether pre-exposure to cold in guinea pigs does increase their resistance to intense cold, because to my knowledge it has never been studied. It is surprising to see that monkeys pre-exposed to cold and receiving 25 milligrams of ascorbic acid do not resist intense cold better than monkeys kept at room temperature receiving the same amount of ascorbic acid. The monkeys constantly kept at 10 C. for at least six months before exposure to the intense cold (−20 C.) have grown a much thicker fur than the ones kept at room temperature yet, the performance of both groups is about the same at −20 C. Such a result is entirely different from the ones obtained on rats and rabbits by Blair and his co-workers (13)

The performance at −20 C. of the group kept at room temperature and receiving the high dosage of ascorbic acid is better based on rectal temperatures than that of both groups receiving 25 milligrams of ascorbic acid, pre-exposed or not to cold. The same group is far behind the one receiving an equal amount of ascorbic acid and pre-exposed to cold, on the basis of the falls in rectal and intramuscular temperature and the incidence of frostbite. It seems that the action of ascorbic acid is at its maximum when there is already a stimulation due to cold.

Kark. Dr Dugal in those two groups, pre-exposed to cold, did they both grow hair?

Dugal Yes

Kark Did you make any measurements of the amount of hair grown by the two different groups?

Dugal No I did not.

Kark The crucial thing may be that when a monkey is exposed to cold, say at +10 C., he grows hair which in turn may increase his requirements for ascorbic acid. If he is given only 25 mg. of ascorbic acid a day he may not have quite enough to grow hair maximally whereas if he gets from 75 to 100 mg. per day then his hair may grow at a maximal rate. It may be that the reason why those given 325 mg. are protected, is that their hair growth is greater

Dugal Well, I don t think so because from what we have seen, it is impossible to note any difference in the growth of hair between those which received 25 mg per day and those which received 325 mg. I know that 25 mg per day of ascorbic acid cover the needs of the monkeys for that substance at room temperature.

Kark I think it would be very nice if you could get some data on amount of hair

Dugal You mean you would just shave them and weigh the hair?

Kark Yes.

Dugal How would you explain then that the group receiving 325 mg. of ascorbic acid at room temperature, not pre-exposed to cold, has done much better as far as rectal temperature is concerned than the pre-exposed group which has grown hair and is receiving 25 mg. of ascorbic acid in the cold when both are exposed to −20 C.? Would it be for the same reason?

Kark I don t know at all.

Dugal They have much less hair at room temperature, even when receiving 325 mg. a day of ascorbic acid. How would you explain the results obtained when we varied the ascorbic acid dosages on the same monkeys continuously exposed to 10 C., especially when the treatment with 325 mg. a day of ascorbic acid preceded the one with 25 mg? From 37 experiments on three monkeys it was shown that the high dosage of ascorbic acid, prior to the lower one, had a beneficial effect for resistance to intense cold, as judged by the maintenance of rectal and intramuscular temperatures and by the ability to avoid frostbite. Would you explain those results on the same basis?

Kark I don t know I am not very much impressed with those small differences in rectal temperature even though they would seem significant.

Blair Of course, in animals the growth of hair is very slight over those areas that are usually susceptible to frostbite. There is much less insulation on the feet, ears, and tail than there is on the rest of the body of the animal. Those frostbitten areas of the ears, feet, and tails actually show little change in hair growth during acclimatization to cold, and I believe the amount of hair to be of only minor significance in resistance to cold injury

Burton: Do the monkeys show any changes in behavior? From their behavior would you say the ones which have been acclimatized to cold and ascorbic acid dislike going into the extreme cold less?

Dugal: No they all disliked being manipulated, so we can t say if it was because they were going to go into the cold or just because we came close to them. They are not tame at all.

POSSIBLE MECHANISMS UNDERLYING THE EFFECT OF ASCORBIC ACID

Dugal: The question now arises as to why ascorbic acid has such an effect during exposure to cold Frankly Mr Chairman, I have no definite answer but I have a few results that point to the fact that at least part of that action is through the hypophysis-adrenal axis. First of all may I present some results (14) showing the relative importance of the adrenal glands in resistance to cold as compared to another stress like muscular work.

You may be aware that it has been found by Selye (15) and others (16) that rats already adapted to cold, when adrenalectomized, resist cold better than adrenalectomized rats not acclimatized to cold. But what about nonacclimatized, nonadrenalectomized rats? Do they resist cold less than the ones already acclimatized but adrenalectomized, as is the case for muscular work? You know Selye has shown that in the case of muscular work, rats which are adapted and then adrenalectomized are more resistant, in fact, than animals with their adrenals. We wanted to see if that was the case with another stress, like cold.

We conducted three experiments which stressed the importance of the adrenal glands, two on resistance to cold, which are summarized in Table XXXII and one on resistance to muscular exercise. The rats had an average weight of about 200 gm. The acclimatized ones were exposed for two months in the cold, before they were exposed to the environmental temperature of 0 C. Twenty-four hours before exposure to cold the rats were adrenalec-

TABLE XXXII

The Effect of Adrenalectomy on Survival of Rats to an Environmental Temperature of 0 C

Group		Treatment	Number of animals	Per cent Survival			
				24 hr	t value	48 hr	t value
First experiment	I	Adapted adrenalectomy	12	41.6%	1.87 (I II)	8.3%	0.39 (I II)
	II	Nonadapted adrenalectomy	17	11.7%	3.41 (I III)	0.0%	4.77 (I III)
	III	Nonadapted sham operation	15	100.0%	4.50 (II III)	100.0%	5.77 (II III)
Second experiment	I	Adapted adrenalectomy	15	46.6%	3.78 (I II)	6.6%	1.32 (I II)
	II	Nonadapted adrenalectomy	23	0.0%	4.20 (I III)	0.0%	0.18 (I III)
	III	Nonadapted sham operation	25	100.0%	7.00 (II III)	100.0%	7.00 (II III)

tomized but left with maintenance supplies of salt and kept at room temperature. These were the same conditions as Selye (15) used for muscular work. The survival of the 12 animals in Group I, adapted to cold and adrenalectomized, is 41 per cent after 24 hours and 8.3 per cent after 48 hours. In Group II the 17 animals, nonadapted to cold but adrenalectomized, had only 11 per cent and zero per cent survival, respectively, after the same periods of exposure. The nonadapted animals of Group III with their adrenal glands intact after only a sham operation survived at the rate of 100 per cent even after 48 hours. The second experiment gave the same results.

From these two experiments, it seems clear that nonadapted animals with adrenals resist cold better than adapted animals without adrenals. Such a result is exactly the contrary to what Selye has found for muscular work. He has never done it for exposure to severe cold though.

Horvath: I am surprised that only 12 per cent of your nonadapted adrenalectomized animals survived 24 hours, because certainly at least in the old experiments that I did with Hartman, we had much better survival than that (17, 18).

Dugal: How much did you get for the adapted animals?

Horvath: We never did study any adapted rats as such. The point is, I am a little disturbed about the relatively small percentage of survival in your nonadapted animals.

Dugal: Well, I think the important point here is that they have all been in the same conditions, and the nonadapted nonadrenalectomized animals survived at the rate of 100 per cent as compared to 41 per cent and 11 per cent for the two other groups respectively.

I am not sure about the temperature in the second experiment. Maybe it was lower than 0° C. We were interested to see what the nonadapted adrenalectomized animals would do in comparison with the adapted adrenalectomized. This confirmed the findings of others that the adapted ones survived better than the nonadapted ones when they were both adrenalectomized.

Horvath: Hartman and I were getting as good survival with our nonadapted adrenalectomized animals as you were getting with your adapted at the same temperature.

Dugal: What was the weight of your rats?

Horvath: They were from 200 to 250 grams.

Dugal: Yours were tougher; that's all.

Horvath: I'm surprised. Well, I don't know. This was ten years ago, and I can forget what we did ten years ago easily enough.

Orr Is it a different breed of rats?

Horvath It could be.

Dugal We repeated the work of Selye (15) on muscular work at the same time, too and we confirmed his results. Table XXXIII shows the resistance to running of the same three groups. Group I ran for 197 minutes and Group II ran for 18 minutes whereas Group III ran for 131 minutes. Here, the adaptation is more important than the presence of the adrenals as Selye found. But in the cold, it seems that the presence of the adrenals is much more important than the adaptation

TABLE XXXIII

The Effect of Adrenalectomy on the Resistance of Rats to Running

Group	Treatment	Number of animals	Resistance in minutes	t values
I	Adapted adrenalectomy	9	197 6 (112 253)	2.46 (I II)
II	Nonadapted adrenalectomy	12	18.6 (8-31)	0 69 (I III)
III	Nonadapted sham operation	7	131.4 (90-176)	2.07 (II III)

Horvath Yes, I agree with that. I don t know about the adaptation as such, but certainly the presence of the adrenals is a very important fact, especially if we can show it another way

Dugal Yes, and it is more important in cold stress than in muscular exercise. That is what I meant.

Having found that the presence of adrenals is important we focused our attention on learning whether the adrenals were important in the action of ascorbic acid during exposure to cold. We studied the relation between the amount of ascorbic acid in different tissues of animals exposed to cold, and their adaptability to the same low temperature, as was measured by the per cent of loss in weight, and the differences between initial and final weight during exposure to cold. It was found (Figure 17) that there was a direct relation between ascorbic acid concentration in the adrenals

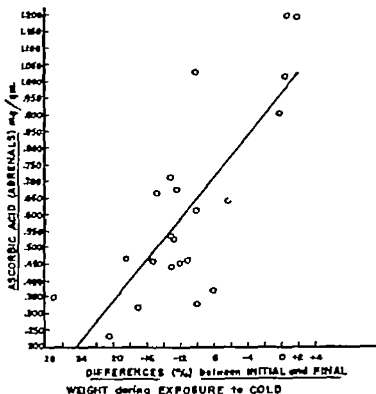


FIGURE 17 Percentage differences between the initial and final weights of the adrenal glands during exposure to cold. Reprinted, by permission, from Dugal, L. P. and Thérien, M.: Ascorbic acid and acclimatization to cold environment. *Canad. J. Res. Sect. E 25, 111 (1947).*

and adaptability to cold. The straight line in Figure 17 has been fitted by the method of the least squares such a relation does not exist at room temperature and does not exist for the livers, kidneys and testes from animals exposed to cold. That result led us to study what would be the influence of large doses of ascorbic acid on the adrenal hypertrophy which is normally observed in animals during exposure to cold.

Table XXXIV shows that for three days exposure (7) to a temperature of —4 C. In the group of rats receiving 150 mg. per day of ascorbic acid the increase in the adrenal weight was very small and not significant. The control group exhibited the normal hypertrophy for such an exposure.

TABLE XXXIV

Treatment	Normal temperature		Cold room (+4 C.)		% increase and t value
	No. of animals	Adrenal weight (mg.)	No. of animals	Adrenal weight (mg.)	
Ascorbic acid 150 mg daily	24	33.45 ± 1.96	33	33.70 ± 1.12	0.74 (0.14)
NaCl – 0.9%	25	32.47 ± 0.97	33	36.09 ± 0.99	11.1 (2.64)

Reprinted, by permission, from Dugal, L. P and Thérien, M. The influence of ascorbic acid on the adrenal weight during exposure to cold. *Endocrinology 44, 420 (1949).*

TABLE XXXV

Treatment	Normal temperature		Cold room (+4 C.)		% increase and t value
	No. of animals	Adrenal weight (mg.)	No. of animals	Adrenal weight (mg.)	
Controls	20	36.63 ± 1.89	20	44.88 ± 2.98	22.4 (2.36)
Ascorbic acid 25 mg daily	20	36.90 ± 1.75	20	37.90 ± 1.15	2.7 (0.56)
Difference	none		18.4% (t=2.18)		

Reprinted, by permission, from Dugal, L. P and Thérien, M. *The influence of ascorbic acid on the adrenal weight during exposure to cold. Endocrinology 44 420 (1949)*

After eight months at 4 C. the adrenal weights of the control group represented on Table XXXV kept in the cold increased 22 per cent when compared to the adrenal weights of the controls kept at room temperature. Of the groups receiving 25 mg. of ascorbic acid daily by mouth, the group exposed to cold had an increase in adrenal weight of only 2 per cent which is not significant. *Incidentally the prevention of hypertrophy by ascorbic* acid during exposure to cold, has been confirmed by Eisenstein and Boniface (19) working at Washington University But even if the hypertrophy of the adrenals were prevented during exposure to cold, the resistance was nevertheless increased towards the same damag-

ing agent. We wondered what was going on with respect to the activity of the adrenals. Was it blocked by the substance that prevented hypertrophy during exposure to cold? We chose to follow the cholesterol changes as an index of the activity of those glands. Because we were giving ascorbic acid, we could not use the AAF (Ascorbic Acid Factor) changes.

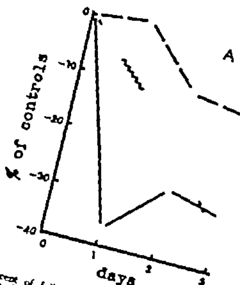


FIGURE 18. The per cent of fall of adrenal cholesterol in animals treated with ascorbic acid and in controls. Reprinted, by permission, from Thérien, M. Leblanc, J., Heroux, O. and Dugal, L. P. Eff ts de l'acide ascorbique sur plusieurs arables biologiques normalement affectés par le froid. Canad. J. Res. Sect. E 27: 349 (1949).

The results obtained in rats show that ascorbic acid increases and hastens the per cent of fall in adrenal cholesterol which may be seen in Figure 18 where the solid line represents the fall in adrenal cholesterol in ascorbic acid-treated (sodium ascorbate) animals. The dotted line is for the untreated controls and the dash line is for the controls receiving injections of sodium bicarbonate. The rats which we used (20) weighed °00 gm. and were exposed to 0 C. There is a fall in cholesterol in all groups, but it is significant in the control groups only after three days whereas it is already significant and very marked, after twenty-four hours, in the group receiving ascorbic acid. Such an effect of ascorbic acid could be considered as an ACTH like effect. Other corticotrophic-like effe...

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NaCl – 0.9%	25	32.47 ± 0.97	33	36.09 ± 0.99	11.1 (2.64)

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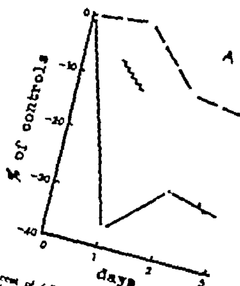


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have been observed in our laboratory for instance, DCA hypertension is prevented by ascorbic acid in normal rats (21) but not in adrenalectomized ones I know that ACTH *does not prevent DCA* hypertension, but I know that cortisone does.

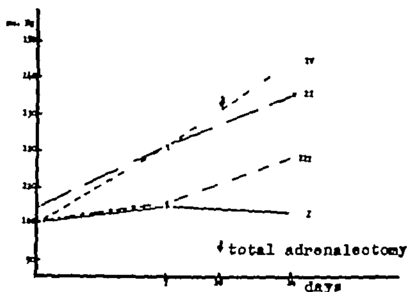


FIGURE 19. The effect of adrenalectomy on elevation of blood pressure in groups of rats *receiving DCA and DCA plus ascorbic acid. Reprinted, by permission, from* Héroux, O., and Dugal, L. P Effet de l'acide ascorbique sur l'hypertension provoquée par l'acétate de désoxycorticostérone (DCA) *Rev. canad. de biol.* 10, 193 (1951).

Figure 19 shows that the elevation in blood pressure is much smaller in the group of rats treated with *DCA plus* ascorbic acid (Group III) than in the one receiving DCA alone (Group II) The difference is significant. But such an effect is not obtained in adrenalectomized animals treated with DCA (Group IV) Group I represents the controls here. Another corticotrophic-like effect of ascorbic acid *observed in our laboratory is that the so-called for*maldehyde arthritis in rats is prevented and cured as effectively by ascorbic acid as it is by ACTH (22)

The ACTH like effects might have been due to a nonspecific stress caused by the large doses of ascorbic acid used but against that *interpretation were the facts that adrenal* hypertrophy was prevented during exposure to cold and that resistance to cold was increased by the same large doses of vitamin C.

We recognized three working hypotheses: *a*) ascorbic acid prevents the hypertrophy of the adrenals during stress because it inhibits directly the action of ACTH, in which case ACTH would be produced just the same (23). We didn't believe very much in such an hypothesis, and, as a matter of fact it was ruled out by the results obtained. The group (D) receiving ascorbic acid and 10 mg. per day of ACTH shows the same increase in adrenal weight after three days of treatment as the control group (B) receiving bicarbonate and the same amount of ACTH (Table XXXVI). The control group in this experiment received sodium bicarbonate with the amount of sodium equivalent to that contained in sodium ascorbate. Ascorbic acid was administered in the form of sodium ascorbate because it is better tolerated by the rat than ascorbic acid itself when given by mouth. The results, for the increase in adrenal weight were the same whether we gave ascorbic acid and ACTH or sodium bicarbonate and ACTH. Therefore we do not prevent the increase in adrenal weight with ascorbic acid in normal animals.

TABLE XXXVI

The Effect of Ascorbic Acid Treatment on the Adrenal Weight of Normal Animals Which Received ACTH

Group	Number of animals	Treatment	Duration of treatment	Adrenal weight mg.	% difference and t value
A	15	$NaHCO_3$	3 days	35.21 ± 1.39	+16.5%
B	16	ACTH — 10 mg + $NaHCO_3$ daily	3 days	41.03 ± 1.33	3.04
C	14	Na-ascorbate 150 mg. daily	3 days	34.91 ± 1.19	+15.[illegible]%
D	16	ACTH — 10 mg. + Na-ascorbate 150 mg. daily	3 days	40.[illegible]1 ± 1.30	3.01

Reprinted, by permission, from Dugal, L. P. and Thérien, M. Effect of ascorbic acid on the adrenal weight of normal and hypophysectomized rats. Science 115, 59[illegible] (195[illegible].)

have been observed in our laboratory for instance, DCA hypertension is prevented by ascorbic acid in normal rats (21) but not in adrenalectomized ones. I know that ACTH *does not prevent* DCA hypertension, but I know that cortisone does.

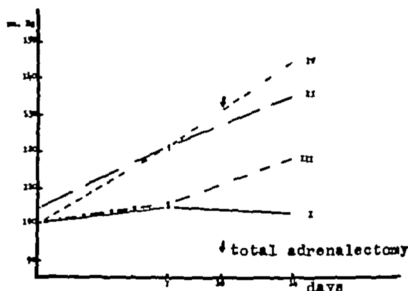


FIGURE 19. The effect of adrenalectomy on elevation of blood pressure in groups of rats receiving DCA and DCA plus ascorbic acid. Reprinted, by permission, from *Héroux, O., and Dugal, L. P.* Effet de l'acide ascorbique sur l'hypertension provoquée par l'acétate de désoxycorticostérone (DCA) *Rev. canad. de biol* 10, 183 (1951).

Figure 19 shows that the elevation in blood pressure is much smaller in the group of rats treated with DCA plus ascorbic acid (Group III) than in the one receiving DCA alone (Group II) The difference is significant. But such an effect is not obtained in adrenalectomized animals treated with DCA (Group IV) Group I represents the controls here. Another corticotrophic like effect of ascorbic acid observed in our laboratory is that the so-called formaldehyde arthritis in rats is prevented and cured as effectively by ascorbic acid as it is by ACTH (22)

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We recognized three working hypotheses a) ascorbic acid prevents the hypertrophy of the adrenals during stress because it inhibits directly the action of ACTH, in which case ACTH would be produced just the same (23) We didn't believe very much in such an hypothesis, and, as a matter of fact it was ruled out by the results obtained. The group (D) receiving ascorbic acid and 10 mg. per day of ACTH shows the same increase in adrenal weight after three days of treatment as the control group (B) receiving bicarbonate and the same amount of ACTH (Table XXXVI) The control group in this experiment received sodium bicarbonate with the amount of sodium equivalent to that contained in sodium ascorbate. Ascorbic acid was administered in the form of sodium ascorbate because it is better tolerated by the rat than ascorbic acid itself when given by mouth. The results for the increase in adrenal weight, were the same whether we gave ascorbic acid and ACTH or sodium bicarbonate and ACTH Therefore, we do not prevent the increase in adrenal weight with ascorbic acid in normal animals.

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Group	Number of animals	Treatment	Duration of treatment	Adrenal weight mg.	% difference and t value
A	15	$NaHCO_3$	3 days	35 .1 ± 1.35	+16.5%
B	16	ACTH — 10 mg + $NaHCO_3$ daily	3 days	41.03 ± 1.35	8.04
C	14	Na-ascorbate 150 mg. daily	3 days	34 91 ± 1 19	+15.2%
D	16	ACTH — 10 mg + Na-ascorbate 150 mg., daily	3 days	40.1 ± 1.30	3 01

Reprinted, by permission, from Dugal, L. P and Thérien, M Effect of ascorbic acid on the adrenal weight of normal and hypophysectomized rats. Science 115, 5?? (1952)

The second hypothesis was *b*) ascorbic acid prevents the hypertrophy of the adrenals during stress because its presence causes a hyperactivity of the adrenal cortex and a hypersecretion of cortical hormones a hypothesis that could have been substantiated at the time by the fact that the fall in adrenal cholesterol is greater with ascorbic acid than without during exposure to cold. The hypersecretion of the cortical hormones would prevent indirectly the hypersecretion of ACTH, according to Sayers theory (24) That second hypothesis was also ruled out by the following experiments. Ten days after hypophysectomy we removed the left adrenal and treated the animal with ascorbic acid for the next ten days at that time we removed the right adrenal, took its weight, and studied it histologically The animals were maintained at room temperature. The control group receiving sodium bicarbonate (Table XXXVII) does not show any increase in the weight of the right adrenal after treatment as compared to the left adrenal before treatment, and the weights are virtually the same for the group receiving ascorbic acid. We have no effect, at least for such a ten-day period of treatment as we have used. Therefore, there is no corticotropic effect of ascorbic acid *per se*

Horvath Isn t it true that without treatment hypophysectomy prevents hypertrophy of one adrenal if the other is removed?

Dugal Yes, but if you have a substance like ACTH, which has a corticotropic effect, that is the way to test it. That is what we wanted to see for ascorbic acid.

The third hypothesis was *c*) *ascorbic acid has a potentiating* effect on the action of ACTH when the demand for cortical hormones increases. Hence, small doses of ACTH corresponding approximately to normal secretions, unable by themselves to hyperactivate the adrenal cortex, would do it under the influence of ascorbic acid. If such were the case, the hypophysis would not be expected to be hyperstimulated in the case of stress, because enough cortical hormones would be produced by the combined action of small doses of ACTH and ascorbic acid. The problem here was to see if ascorbic acid could potentiate the action of ACTH, and the results obtained show that apparently it is so.

A dosage of 0.5 mg of ACTH per day intraperitoneally was used in hypophysectomized rats. The conditions of this experiment were the same as in the preceding one, namely that we waited about fifteen days after hypophysectomy to have complete atrophy of both adrenals. Then we removed the left adrenal, weighed it, and analyzed it histologically (Table XXXVIII) The ACTH was all

TABLE XXXVII

A Comparison of the Changes in Weight of the Adrenal Gland Following Hypophysectomy in Ascorbic Acid Treated and Control Animal

Treatment	Time since hypophysectomy	Time between left and right adrenalectomy	Duration of treatment	Number of animals	B. W. gm. Initial	B. W. gm. Final	Mean w. (mg.) L. adr.	Mean w. (mg.) R. adr.	Thymus weight mg.	Thyroid weight mg.
NaHCO	16 days	5 days	10 days	9	10_5	103.8	5.10	5.1_	150.0	4.09
Na-ascorbat	16 days	6 days	10 days	9	10_3	101.3	5.09	4.84	100.3	5.01
% difference between								−1.9	+1_8	+1.0

Reprinted, by permission, from Dugal, L. P. and Thérien, M. Ascorbic acid and acclimatization to cold environment. Canad. J. Res. Sect. E 25, 111 (1947)

TABLE XXXVIII

A Comparison of the Effects on Adrenal Weight of Small Doses of ACTH Alone, and ACTH Plus Ascorbic Acid in Hypophysectomized Rats

Treatment	Duration of experiment after hypophysectomy	Duration of treatment	Number of animals	Mean adrenal weight (mg.)		Difference between L. and R. adr	
				L. adr	R. adr	Absolute (mg.)	%
ACTH 0.5 mg. daily	20 25 days	7 10 days	19	5.99	5.73	0.26	4.3
$NaHCO_3$ + ACTH 0.5 mg. daily	25 days	10 days	10	5.53	5.28	0.25	4.5
Na-ascorbate 150 mg. + ACTH 0.5 mg. daily	20 25 days	7 10 days	21	5.79	7.27	1.48	25.6 t=3.61
% difference between R. adrenals of diff. groups			between 1 and 3 26.9 (t=2.79)			between 2 and 3 37.7 (t=4.54)	

Reprinted, by permission, from Dugal, L. P. and Thérien, M. Effect of ascorbic acid on the adrenal weight of normal and hypophysectomized rats. Science 115 598 (1952).

from the same batch and number. We treated the first group with ACTH, 0.5 mg. for seven days in one series and in the other ten days. There is no hypertrophy of the right adrenal with that dosage of ACTH alone, nor is there any decrease in sudanophilia or any increase in the cortex section as measured with a planimeter (23,25).

The second group was treated with the same dosage of ACTH and sodium bicarbonate; the results obtained are the same as for the group receiving ACTH alone. The right adrenal after treatment is not larger and does not show more activity than the left adrenal before treatment. It is a decrease rather than an increase in both cases, but it is about the same. Finally, the last group received 0.5 mg. of ACTH plus ascorbic acid; after seven or ten days of treatment, the right adrenal shows an absolute increase in weight of 1.48 mg. as compared to the left adrenal before treatment. It corresponds to an increase of more than 23 per cent and this is highly significant.

Kark: Were all those experiments done at the same time?

Dugal: Yes, they were.

Figure 20 shows in part 1 a comparison of sudanophilic material between a section of a left adrenal of a hypophysectomized rat, before treatment, and in part 2 a section of the right adrenal of the same rat, after treatment with ACTH plus ascorbic acid. The depletion of sudanophilia is especially evident in the *zona fasciculata*. There is no such depletion in the right adrenal of rats treated with ACTH alone (0.5 mg.) or with ACTH (0.5 mg.) plus sodium bicarbonate; in the two latter cases, the picture shown by the right adrenal would be the same as the one that we have here for the left adrenal. All those results seem to show that ascorbic acid potentiates the effect of ACTH or, if you prefer, increases the receptivity of the adrenals for ACTH.

Another problem presents itself and that is how exactly to relate the fact that ascorbic acid has such an action on the hypophysis-adrenal axis to another fact, namely, that it increases resistance to cold, because after all we will eventually have to explain the beneficial effects of ascorbic acid for resistance to cold as being due either to an increase in heat production, or to a decrease in heat loss.

For that purpose one of the things to do is to measure the metabolism of our monkeys under the same experimental conditions. We have also underway a new series of experiments on tissue metabolism; the results obtained so far are sufficiently clear to show that the fall in glycogen content of the liver during exposure to cold, is greater in the ascorbic acid group than in the control



FIGURE 20. (1) Section of left adrenal of a hypophysectomized rat before treatment. (2) Section of right adrenal of the same rat after treatment with ACTH plus ascorbic acid. Reprinted, by permission, from Des Marais, A., and Leblanc, J.: In vivo and in vitro effect of ascorbic acid and ACTH on the rat adrenal cortex. *Canad. J. M. Sc. 30, 157 (1952).*

TABLE XXXIX

The Effect of Ascorbic Acid Administration on the Liver Metabolism and Glycogen Content of the Liver in Animals Exposed to Normal and Cold Temperatures

Group	Treatment	Oxygen uptake		Glycogen content	
		qO_2 ± S.E.	% from A	mg./100 mg. ± S.E.	% from A
A	Normal temperature	(14) — 8.34 ± 0.[illegible]2	—	(10) 5.20 ± 0.31	—
B	Normal temp + asc. acid	(15) — 8.45 ± 0.16	+ 1.1	(17) 4.81 ± 0.25	— [illegible]3
C	Cold room	(15) — 9.38 ± 0.30	+1[illegible]	(15) [illegible]03 ± 0.35	—43.3
D	Cold room + asc. acid	(15) — 10.13 ± 0.23	+25.1	(17) 1.91 ± 0.30	—63.5

Between	Oxygen uptake		Glycogen content	
	Diff ± S.E.	t	Diff ± S.E.	t
A B	0.11 ± 0.27	0.41	0.30 ± 0.40	0.9[illegible]
A C	1.02 ± 0.5[illegible]	–[illegible]8	—[illegible]5 ± 0.1[illegible]	4.[illegible]9
A D	–.09 ± 0.1[illegible]	0.51	2.89 ± 0.37	8.80
C D	1.0[illegible] ± 0.39	–.52	1.01 ± 0.40	2.00



FIGURE 20. (1) Section of left adrenal of hypophysectomized rat before treatment. (2) Section of right adrenal of the same rat after treatment with ACTH plus ascorbic acid. Reprinted, by permission, from Des Marais, A. and Leblond, J.: *In vivo* and *in vitro* effect of ascorbic acid and ACTH on the rat adrenal cortex. *Canad. J. M. Sc.* 30, 157 (1952).

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		qO_2 ± S.E.	% from A	mg./100 mg. ± S.E.	% from A
A	Normal temperature	(14) — 8.34 ± 0.[illegible]2	—	(10) 5.90 ± 0.31	—
B	Normal temp. + asc. acid	(15) — 8.45 ± 0.16	+ 1.1	(1[illegible]) 4.81 ± 0.25	— [illegible]5
C	Cold room	(15) — 9.36 ± 0.30	+12.2	(19) [illegible].95 ± 0.35	—43.3
D	Cold room + asc. acid	(15) — 10.43 ± 0.23	+25.1	(17) 1.91 ± 0.30	—63.3

Between	Oxygen uptake		Glycogen content	
	Diff ± S.E.	t	Diff ± S.E.	t
A B	0.11 ± 0.27	0.41	0.39 ± 0.40	0.97
A C	1.02 ± 0.37	[illegible]6	[illegible].25 ± 0.47	4.79
A D	[illegible].09 ± 0.3[illegible]	6.54	3.29 ± 0.37	8.89
C D	1.07 ± 0.38	2.8[illegible]	1.04 ± 0.40	2.60

exposed to cold (Table XXXIX) also that the liver metabolism, already increased by exposure to cold (as shown by Sellers) (16) is increased much more in the ascorbic acid treated group (26)

The fall in liver glycogen (Table XXXIX) in the controls exposed to cold for 8 days, Group C, is 43 per cent, but when the animals receive ascorbic acid at the same time it is 63 per cent. There is also an increase in liver oxygen consumption of 12 per cent in the controls exposed to cold, and of 25 per cent in the rats also exposed to cold and treated with vitamin C. Those differences are all statistically significant.

Hegnauer What was the duration of exposure in those experiments where you got the 63 per cent drop of glycogen?

Dugal That is 8 days

Burch What has happened to the body weight of the animals during this time?

Dugal They lose weight to start with and then they gain weight again

Burch Could it be due to edema? Some of the adrenal hypertrophy could be fluid. I was wondering if there could be some difference in vascularity

Dugal No We have compared wet and dry weights of the adrenals and the results were the same in each case.

Kark Dr Dugal if I understand you, when your rats were exposed to cold, the ones who were given high amounts of ascorbic acid did not have an increase in the adrenal weight?

Dugal That is right.

Kark I think I can offer a fourth explanation. I don't know if it's right, but in rats, if you inject ACTH you will increase the adrenal size. In man if you inject ACTH you will not increase the adrenal size. In rats, the adrenal manufactures ascorbic acid, but in man, the ascorbic acid comes from the diet. Therefore, when you give rats 300 mg. of ascorbic acid, the adrenals do not need to hypertrophy to manufacture ascorbic acid.

Dugal No and I agree with you there. That would have been my first explanation. Don't you think it is paradoxical, however that when a small amount of ACTH plus ascorbic acid is given, there is a regeneration in atrophied adrenals? It is not hypertrophy but it is an increase in weight. I know that the two effects obtained with ascorbic acid, namely the prevention of hypertrophy of the adrenals in normal animals exposed to cold, and the regeneration of atrophied adrenals, seem to be contradictory I have been trying to find an

explanation for that, and up to now I have only a speculative one to offer I would say that we have to dissociate the effects of what the English call the ACF the adrenal cholesterol factor from the ones of the AWF the adrenal weight factor

Kark: What about your distribution curve of adrenal weights? How many animals did you use?

Dugal Our results are based (7) on more than one hundred animals and they have been confirmed by Eisenstein and Boniface (19) The fact that ascorbic acid potentiates the action of ACTH (23) also has been confirmed, indirectly Bozović and Milković working in Zagreb just published in the *Lancet* (27) that they found a synergistic action between small doses of ACTH and ascorbic acid, when studying formalin arthritis in rats. They also tried the combined effect of cortisone and ascorbic acid, but had negative results. On the assumption that the effect of ascorbic acid on the hypophysis-adrenal axis might be attributable more to its action at the periphery than on the adrenals themselves, we also tried the effect of ascorbic acid plus cortisone on the resistance of rats to cold. Rats so treated were much less resistant than the controls. Those results, based on experiments that remained at the preliminary stage were never published.

Crismon It seems rather curious that the adrenals would respond to a luxury supply of vitamin C in this way In guinea pigs at least, it has been reported that if one turns the experiment about and depletes the animal of vitamin C by putting him on an ascorbutic diet, one cannot detect any evidence of diminished adrenal cortical function.

Dugal I know that, but it has also been reported by Eisenstein and Shank (28) that there was a hypertrophy of the adrenals in this instance They found that the weight of the adrenal glands of guinea pigs on graded levels of intake of ascorbic acid varied inversely with daily intake of that vitamin. In other words, scorbutic guinea pigs had adrenal hypertrophy They interpreted that, as I recall, as being due to a nonspecific stress, the lack of ascorbic acid being a nonspecific stress. But I would like to know how they define a nonspecific stress After all is it not a lack of cortical hormones due to a greater demand?

Crismon The criterion that was used was not adrenal size in the experiments I have seen reported I have not seen the original article but it reported the response of another index of adrenal cortical function to the injection of epinephrine I believe eosino-

penia was used. Did I understand that Dr Kark said that in the rat the adrenal manufactured vitamin C?

Kark That's right.

Dugal In all animals except man monkeys and guinea pigs, that I know of The rat does synthesize ascorbic acid and always has enough normally

Crismon Has it been shown that the vitamin C source in the rat is not in the gastrointestinal bacteria?

Kark Not as far as I know

Crismon But it seems to me that I recall that the use of antibiotics or sulfa drugs in rats permits one to produce very nice examples of scurvy and the drugs were of the sort that control growth of common denizens of the gastrointestinal tract. While some vitamin C may be synthesized by the rat adrenal cortex, it seems unlikely that this furnishes the entire supply required by the animal. Adrenalectomized rats maintained on DCA or salt and vitamin C-free diets do not develop scurvy Müller has reported that adrenalectomized mice show reduced liver vitamin C but these levels return toward normal in animals maintained for more than a month (29 30 31)

Burton Is there not suggestive evidence that you cannot produce scurvy in humans by deprivation of vitamin C unless there is cold also?

Horvath Well, John Crandon (32) a couple of years ago had to be on a completely vitamin C-deficient diet for a period of six months before he developed signs of scurvy

Dugal In the cold?

Horvath No, normal environment.

Burch Isn t that true for almost any vitamin deficiency? It has been found to be almost impossible to produce pellagra in patients with niacin.

Horvath It certainly was an extensive period of time that Crandon had to be on this completely deficient diet before he showed any signs of deficiency

Kark The English experiments too showed that. They had to be on the diet for from 6 to 12 months.

Dugal I am not debating it for humans except that there is an experiment which has just been terminated at the Defence Medical Research Laboratories in Toronto which was conducted on two groups of human subjects, one group receiving 300 mg a day of ascorbic acid, the other 25 mg., the dosage advocated by the British. Those subjects clad only in shorts, were exposed constantly

for 11 consecutive days at a temperature of 60 F. Although the results are not completely analyzed statistically, some are clear enough to show that the group on the low ascorbic acid dosage was pretty miserable as compared to the other one.

Burton: Also, has it not been pointed out in the old records of *voyageurs* such as Jacques Cartier that scurvy was so prevalent on sea voyages in the North Atlantic where they were without a source of vitamin C, that they didn't even bother reporting scurvy?

Dugal: Yes, that is true.

Kark: Well, Captain Cook had scurvy in the South Seas. Capetown was founded to provide vegetable farms for curing scurvy in galleons of the Dutch East India Company.

Burton: It was cold down there, wasn't it?

Kark: No, they got scurvy by going from Holland to Capetown.

Dugal: Well, you know what happened in 1534 in Quebec when Jacques Cartier came in. They were all dying of scurvy just two months after they had settled there. It didn't take long there.

Burton: How long does it take a guinea pig to develop symptoms of scurvy?

Dugal: Three weeks.

Burton: Is that changed if you put him in the cold?

Dugal: Oh, yes. Then they die in about four or five days. It depends of course on the weight of the guinea pigs.

Burton: Do they die showing symptoms of scurvy or just die from cold?

Dugal: No, they do show symptoms of scurvy, in the joints, for instance.

Talbott: Dr. Burton, will you tell us more about the action of the liver as a source of energy?

THE ACTION OF THE LIVER AS A SOURCE OF ENERGY

Burton: Some of the remarks I have to make are just impressions I have gained from putting various things together speculatively and from reading the literature. My own conviction is that it is worth while to look at the liver as the important source of heat in acclimatization.

I have always been impressed with the very old work which was reported by Julius Lefevre (33) on the hibernating animal who goes to sleep with his tissues full of fat; at the end of the winter the animal has lost the fat from its peripheral tissues and has a liver packed full of glycogen. Within two hours after awakening he will become warm-blooded. During that abrupt rise of temperature the

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temperature of the liver and the front part of the body is as much as 10 degrees higher than that of the rest of the body so it seems quite evident that the heat which warms him so quickly the rewarming heat, is coming from chemical action in the liver This is suggestive that the liver in hibernating animals can be a very important source of heat. Obviously we should not carry this over to the homotherms because there is good evidence that the true hibernators are not homotherms in the usual sense even when they are in the warmblooded state Again, the liver I think, is a pretty important source of heat in normal metabolism. The liver temperature normally is from a quarter to a half a degree higher than the rest of the body Considering the very good heat exchanges in the center of the body I think that must mean that there is considerable heat produced.

Then, there is the evidence that Dr Dugal has told us of, in which You and Sellers (34) have shown that slices of livers of *acclimatized rats in the Warburg apparatus, have an increased* oxygen consumption. Dr Campbell, of Toronto who at the time was not particularly interested in cold at all, injected rats day after day with a dose of anterior pituitary extract and, after a week, killed them serially and found the oxygen consumption of liver slices up three or four times.

Dugal The clipped rats of Dr Sellers had an increase of about four times. That was for the whole animals, not for the liver slices (16)

Burton Four times what it started from would certainly show that under that kind of hormonal stimulation, the liver metabolism and presumably the liver heat can be raised to fantastic heights as compared with the normal.

I wish I were certain whether or not the heat production of acclimatized rats is maintained in the cold at a considerably higher level than for the first few days in such rats before they are acclimatized. This has been reported by Sellers and You (35) but I think they tend to contradict it later I myself am not at all sure what the answer is I thought at first this was proved, but I don t know what to think now However the reports have come in that this is so. It seems to me extremely difficult to see how these acclimatized animals are maintained at the higher temperature, whereas the temperature of the unacclimatized animal is allowed to fall in the cold, unless the acclimatized animals are capable now of producing a much greater rate of heat production The only other

possibility would be that they are much better insulated, and that does not seem to be so

If this heat production is increased so much, then I begin to wonder how When one puts an animal in the cold, the acute reaction is for the metabolic rate to rise from two and one-half to three times the normal resting rate· this is thought to be in the larger animals at least, due to neuromuscular activity of thermal tone and shivering in the muscles. It is difficult for me to conceive that such a neuromuscular mechanism could be so adapted that now the muscles could continuously produce much more heat going full blast than they were before. It makes me look for some other place for this extra source of heat.

It seems to me that the indications are that this might be the liver but, as I say more experiments have to be done on oxygen consumption and heat production of animals that we acclimatize to the cold, to verify whether or not the continuous heat production is greater than it was in the first few days. I asked Dr Carlson about this and found that he had done a few experiments with direct heat measurements on rats I think his answer was that he had not found that this heat production was increased However I don t think he had enough to give a final answer

Blair There is a very good possibility that both factors may be coming into play both the liver and the shivering or neuromuscular activity I am sure that Dr Dugal is familiar with the papers of Dr Chevillard (36) in Paris, in which he described rather marked hypertrophy of the liver in rabbits which had been exposed to cold for a long period. We were rather intrigued with his findings. If I can recall them correctly I believe he found about five per cent increase in liver weight following exposure to cold. We checked his figures very carefully in our acclimatized rabbits, and we have seen a little greater hypertrophy in those rabbits acclimatized to cold for 50 days as compared to control animals. We rather suspected, as Dr Burton suggested, that this hypertrophy of the liver may have something to do with heat production, but we have no figures to substantiate that. It was not edema of the liver because we determined both dry weight and wet weight of the liver and it was a true tissue hypertrophy

In relation to neuromuscular action, I am not sure but feel fairly certain that these animals which have been conditioned by acclimatization to shivering for a long period of time continue to shiver more efficiently and longer without fatigue. We noticed in rats and rabbits by visual observation that initially both groups

started shivering rather vigorously and while that was going on, colonic temperatures remained normal. Then we noticed that the nonacclimatized animals appeared to become fatigued to the point where their shivering could no longer be observed whereas the coldacclimatized animals kept on shivering vigorously. When that occurred, colonic temperatures of nonacclimatized animals began falling and hypothermia developed. Thus, we suspect that most of the increased heat production is due to the ability of the acclimatized animal to continue shivering at a very high rate without fatigue.

Burton Have you any knowledge about blood sugar at the time they stopped shivering?

Blair No we have no knowledge on that.

Burton *As you know the lowering of blood sugar will inhibit* shivering, as Cassidy *et al.* (37,38) showed. Also the injection of a small amount of insulin will abolish shivering. I was wondering if *once again, the liver was involved, that somehow or another* the liver can keep the blood sugar up better so the animal can go on shivering.

Blair *That is a possibility but we have no blood sugar determinations.*

Burton Perhaps I could report two things that come to my mind. *Dr G Malcolm Brown, of Queens University on his expedition* to Chesterfield Inlet four or five years ago, found that the livers of the Eskimos up there in the spring were clinically extremely enlarged. *He managed to get some twenty liver biopsies* and the pathologist at Queens University after studying them for a couple of years came to the decision that he could find nothing pathological *about them, except that they did seem to be extremely* full of glycogen

The second thing on which I cannot report finally because it is just by hearsay from *Professor Rossiter Professor of Biochemistry* at the University of Western Ontario is that he has students studying the radioactive phosphorus of the liver of rats left in the cold, and he is rather *disappointed to find that they can detect no* change in the radioactive phosphorus uptake, as an indication of liver activity. This does not mean, of course there may not be other *activity in the liver*

Dugal His group found a change in the adrenals, though the turn over was greater

Blair *I might mention also that we made microscopic* sections of the hypertrophied livers of the coldacclimatized animals and the

livers of the nonacclimatized, as far as we could detect from these histological studies they were absolutely identical. We could find no difference at all.

Crismon No increase in glycogen?

Blair Not as far as we could tell. We examined the tissues very carefully and we could observe no difference at all in the sections. Of course, a six per cent increase is not an extremely large hyper trophy and one would not expect to find too much change.

Crismon Six per cent?

Blair About six per cent was our degree of hypertrophy

Crismon That is distinctly within the range where glycogen increase would account for the entire change in size. It puts one in mind of another stressful circumstance that is responsible for accumulation of glycogen in the liver namely high-altitude ex posure with low CO in the respired atmosphere, as demonstrated by Langley and Clark in rats and by Thorn and others in dogs.

With regard to li er qO_2 measurements, it is of some importance to correct respiration values for tissue glycogen content rather than simply to rely on either wet weight or dry weight as a means of expression, because glycogen is an extremely labile solid constituent of liver If the correction were made, I imagine that these figures of Dr Sellers and others for increases in liver qO_2 would be even more striking than those they reported.

Talbott Could the increase in glycogen content increase the oxygen consumption in the rabbits four times?

Crismon: No I didn't mean to imply that, Dr Talbott. What I meant was this you may demonstrate that the oxygen consumption, on a wet-weight or a dry weight basis, of the livers of animals treated in any given way is higher than that of controls by a matter of four times. A high liver glycogen content provides an inert substance contributing to the tissue weight. If you eliminate that inert substance in the final calculation and consider only the remainder then you have another factor which further expands the difference between the controls and the experimental animals. The studies of Fuhrman and Field (39) show that doubling the glycogen content of liver from 4 per cent to 8 per cent with its accompanying water reduces the apparent qO_2 by 18.7 per cent. It is obvious that the fourfold increase mentioned by Dr Dugal, in animals that presumably had high liver glycogen must be somewhat smaller than the actual increase if it were calculated on a glycogen-free basis.

Talbott I thought Dr Burton's comment concerned more a

change in the biochemical reaction rather than the pure deposition of glycogen in the liver

Crismon Need these things be mutually exclusive? I think they may well occur together

Talbott That is true. If it were purely an increased glycogen content, could that alone account for this increase?

Burton Thermodynamically there is a large amount of heat liberated when glycogen is turned into blood sugar This does involve a pretty large increase of heat.

Crismon Do you know the thermodynamics of glycogen liberation, Dr Burton?

Burton No I don t, I imagine it is the other way

Crismon I don t know The liver derives a good bit of its energy I understand, from oxidative deamination, or at least the downstream effects of deamination. With amino acid as the only substrate isolated kidney tissue will carry out very brisk oxygen consumption to furnish energy

Burton Dr Rossiter is most anxious to study the radioactive traces in the nitrogen content of the liver but, of course, this is extremely difficult as compared with the study of radioactive phosphorus.

Crismon I would like to ask Dr Dugal if he has any speculations concerning the details of the role of ascorbic acid in this pattern he has described. Could it be that of a coenzyme?

Dugal Well, that is a possibility but we don t know We haven't done anything yet along that line, except on the liver And even there, it was not by adding ascorbic acid to the liver slices. Ascorbic acid was given to the whole animal exposed to cold, and then we made liver slices and studied the oxygen uptake. It is possible, however that it does act in the oxidative reactions of the cell as a coenzyme.

Crismon Certain of the metabolic defects seen in isolated tissue from scorbutic animals, can be repaired *in vitro* by the addition of ascorbic acid. That has been reported in this country (40) and in Japan, where Suda and his associates have found that some of those defects can be equally well repaired by the addition of ferrous ion (41)

Dugal Masson, working in the Cleveland Clinics, Schaffenburg and Corcoran (42) showed that they could repair or at least prevent the effects of scurvy with cortisone. What we have been working on is the association of ascorbic acid with ACTH or cortisone or both, and the related effects on the functions of the

adrenal-hypophysis axis. I don't want to be too specific, regarding the interpretation of our results.

Burton: My difficulty is that apparently one may use the depletion of cholesterol or the depletion of ascorbic acid from the cortex as an indication of the activity of the adrenal gland.

Dugal: Oh, yes.

Burton: Now that has always puzzled me very much. If it were acting as an enzyme why should it decrease so much when the activity of the gland increases? On the other hand, biochemically surely it is very difficult to see how it could act as any sort of a precursor for the steroids. Have you any suggestions at all?

Dugal: No. All the observations concerning the effects of ascorbic acid on the activity of the adrenals do not exclude necessarily themselves. There may be a lot of apparently independent actions: enzyme activity, potentiation of ACTH, action at the periphery etc., but I would be at loss to relate them. As to the fact that ascorbic acid might be a precursor of the steroid hormones, I do not believe that there is any evidence for it.

Burch: Is there likely to be some other substance that might do the same, such as glutathione?

Dugal: We tried other substances. We tried methylene blue, without much result. I may add that when we were titrating ascorbic acid in rats exposed to cold, we found that its concentration did increase in the tissues of those animals that succeeded in getting acclimatized, as I mentioned previously. But we were aware then that the increase of ascorbic acid observed might have been only apparent and due to an increase of substances like glutathione; however, that objection was eliminated by using the method of Bessey and King (43) which is supposed to be specific for ascorbic acid, when you operate at a pH of about 4.8, using metaphosphoric acid for that purpose.

There is one other question that might arise. Since the rats which synthesize ascorbic acid eat more when they are exposed to cold, it is possible that the increase in the ascorbic acid concentration of their tissues, during exposure to cold, might be due only to the fact that they eat more; in such a case it would not be possible to interpret the increase in ascorbic acid as being a defence reaction due to cold. To answer that question, we tried the effect of cold on fasting animals. We froze the tails of fasting rats, and we got the same increase (44).

Burton: I was wondering if Dr. Blair would tell us something

about the experiment in Fort Churchill, Canada, on the excretion of ascorbic acid, using the soldiers stationed there?

Blair I think Dr Kark should tell you since it was the Medical Nutrition Laboratory that carried on the studies and since Dr Johnson and Dr Kark's findings on Exercise Musk Ox were used as the basis for the observations

Kark The results from the Fort Churchill experiment were never published. As far as they have been analyzed and as far as the data from Musk Ox have been analyzed, there doesn't seem to be very much change in ascorbic acid metabolism in man exposed to cold, based on blood level and urinary excretion determinations.

Blair Together with observations of ascorbic acid intake

Dugal But, Dr Kark, didn't you report at last year's conference that there was a decrease in ascorbic acid excretion during the Musk Ox expedition? (45)

Kark We are not talking about the Musk Ox expedition now

Dugal But in the Musk Ox expedition there was?

Kark In that one at the time when the soldiers were moving from a very cold to a warmer environment, the blood levels remained the same but the urinary output was less.

Dugal In the studies at Shilo there was an increase wasn't there?

Kark Nothing very significant happened in Shilo at all. That was a 12-day study under much more rigorous conditions of cold.

Burch Dr Blair wasn't ascorbic acid fed to some of the people studied in Alaska, or at Fort Churchill?

Blair There has been some study on feeding ascorbic acid. In fact, ascorbic acid at different levels was fed in the study at Fort Churchill that Dr Kark referred to but the findings were not very significant and were never published.

Burch And it produced no difference?

Kark Apparently not, as far as the data were analyzed, but that whole study needs to be repeated.

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PATHOPHYSIOLOGY OF COLD INJURIES

JACK ADAMS RAY
Department of Surgery
Karolinska Institute
Stockholm Sweden

AN UNDERSTANDING OF how cold kills tissue is extremely important for prophylaxis and the treatment of cold injury One might ask, is there only a true *thermal injury alone or is there a combination* of this with vasomotor disturbances? Dr Shumacker (1) told us last year when speaking of rapid freezing and thawing of frozen skin that such frozen skin *when reapplied as autogenous grafts* to the donor dog would survive. You can look at this experiment from another point of view namely that of the skin being rescued from post freezing vascular reactions that might have killed it.

Dr Kreyberg (2) a Norwegian friend of mine has done some interesting experiments relating to frostbite. First, he has frozen the skin of mice to −78° C. with carbon dioxide snow and he got 100 per cent necrosis of the frozen area (Table XL.) As a second control he transplanted normal epithelium subcutaneously without freezing it, in 30 animals After 12 days the epithelium in 22 of these controls was living and proliferating when seen microscopically He then froze skin areas in 22 animals with carbon dioxide snow and immediately upon thawing transplanted the piece of skin which had been frozen subcutaneously in another place on the same animal. After 12 days 14 of the epithelial transplants survived (Figure 21) about the same percentage as in the normal controls. When he repeated the experiment but waited 3 hours and 45 minutes after thawing to make the transplantation there was survival in fewer skin transplants. When 5 hours elapsed between thawing and transplantation there was still less survival, but some transplants did survive. He ascribes this difference in survival in those transplanted immediately to the avoidance of the postfreezing *vascular reaction, especially the true stasis.*

Figure 22 shows the same thing that Dr Crismon talked about at the last conference When you have had freezing, the circulation will be all right for some minutes and *will then slow down.* There will be a conglomeration of the blood corpuscles, and then

TABLE XL

Control I	Total Number	Number of Animals with Necrosis
Ear frozen with CO_2 snow for 5 sec. and examined 7 days later	48	48
Control II	**Total Number**	**Number with living epithelium**
Transplantation of normal epithelium	30	22
Experiment	**Total Number**	**Number with living epithelium**
Transplantation of frozen epithelium done immediately after thawing	22	14
Transplantation 3 hr to 5 hr and 45 min. after thawing	12	3
Transplantation 5 hr and 20 min. to 6 hr after thawing	20	5

(Translation) Reprinted, by permission, from Kreyberg, L. *La stase et son rôle dans le développement de la nécrose. Acta path. et microbiol. scandinav. Suppl. 91, 40 (1950)*

there will be a true stasis, and the part that has been frozen will be shut off from the circulation.

The connection between cold injury and burns, also discussed at the last conference, has also interested Dr. Kreyberg (3) who has studied the local reaction to heat injuries in the live tissue of mice. He was of the opinion that part of the necrosis is caused by direct action of the heat and part is caused indirectly by the development of stasis followed by ischemia, as a vascular response to heat. That the onset of stasis is followed by necrosis of the entire depth of the skin has also been pointed out by Sevitt (4).

Both Dr. Shumacker and Colonel R. B. Lewis seemed to agree at the conference last year that the benefit of rapid rewarming was not primarily due to the shortening of exposure time to the cold,



FIGURE 21. A bit of skin frozen to −78 C, transplanted subcutaneously and examined 12 days afterwards. Epithelium living and proliferating. Reprinted, by permission, from Kreyberg, L. La stase et son rôle dans le développement de la nécrose *Act path. et microbiol. scandinav. Suppl.* 91 *40 (1950)*.

but it might be due to an alteration in the pattern of local blood flow How I don t know But it is also possible that in rapid warming, the tissue passes rapidly through the stage of 10 C. to 15° C., in which temperature range Lake (5) using tissue cultures, and Kreyberg (6) using living tissue have seen serious damage.

I have been studying the effect of rapid rewarming in man (7) the effects of rapid rewarming on animals have been beautifully shown by American authors. With the permission of patients who were going to have an amputation at the thigh because of gangrene of the foot or the toes using ethyl chloride I froze the skin on the medial and lateral aspects simultaneously for from 2 to 7 minutes just below the site of the planned amputation. I emphasize that the skin was frozen and white for the same length of time on the medial side as on the lateral side. Then I immediately warmed up one side to 37 C. I am told, I should have reached 42 C. I will do it the next time. I did not treat the other side at all, but let it thaw out under the bedclothes. About five minutes after the leg has been put under the bedclothes the bed temperature will be about 28 C.



FIGURE 12. The ear of rat was frozen for 5 seconds with carbon dioxide snow and some days later China ink was injected intravenously. Note the ink does not enter the zone of stasis. Reprinted, by permission, from Kreyberg, L. La stase et son rôle dans le développement de la nécrose, *Acta path. et microbiol. scandinav.* Suppl. 91 *40 (1950).*

After 24 hours, it was possible to see macroscopically that in most cases there was greater damage and more blister formation on the side that was slowly thawed. Bits of skin were excised and sent to my pathologist, Dr Falconer who was not told which had been rapidly thawed and which had been thawed slowly.

Burch: How long were they frozen before they were thawed?

Adams-Ray: I had different lengths of time ranging from 2 to 7 minutes. Dr Falconer looked for blister formation degenerative changes, inflammatory changes, etc. He told me that in 3 cases out of 21 he could see no difference- in 3 other cases there was more damage by the rapid warming, and in 15 cases there was more damage by the slow thawing. With his permission the slides were submitted to another pathologist who was of the same opinion. There is no doubt that there is more pathologico-anatomical damage by slow thawing than by rapid thawing.

Webster: When you say damage what do you mean?

Adams-Ray Degenerative changes and blister formation. There were definite degenerative changes not only in the epidermis but also in the epithelium of the sweat glands and so on. The pathologist couldn't see anything at all in the vessels.

Burch Did you make an effort to prepare the skin in any way such as removing the sebaceous secretions?

Adams Ray No.

Burch Do you have data on the depth of freezing and the temperature levels reached?

Adams Ray No

Burch You just used an ethyl chloride spray?

Adams Ray Yes. The nozzle was held at the same distance on both sides.

Burch But you don't know whether or not the spray was the same?

Adams Ray No

Burch I mention this since we once tried to freeze the skin by Sir Thomas Lewis method with the copper rod and found it remarkably difficult. At times the temperature of the copper rod reached −20 C. with no freezing in another area of skin held in contact with the rod for the same length of time at the same pressure, a nice frozen button developed. The point is that equal freezing is difficult to achieve by such methods

Adams Ray We counted the time of freezing from the time the skin became white and frozen.

Burch You did not place a thermocouple under the skin to learn the depth of freezing in the tissues and levels of temperature reached?

Adams-Ray No. Most of the patients had endarteritis, but one girl aged 15 had a sarcoma. When her skin was frozen, she was among those who showed more damage with slow thawing.

Brinkhous What was the time interval between freezing and the time when you took your biopsies?

Adams Ray Twenty four hours. Somebody asked me if we couldn't do that in a longer interval, because he had seen some vessels after freezing, creep into the tissue Was that you, Dr Crismon?

Siple: Was it possible to observe the colloidal character of the cells between the two periods?

Adams-Ray I have no slides, I am sorry

At this point I would like to present for discussion a point of view that I could not find mentioned at the last conference We all know the vasoconstricting power of cold and we also know that vasoconstriction alone without cold, can kill tissue. From experience with man and from experiments on animals, we know that ergotamine and adrenalin can kill tissues by vasoconstriction alone. A Swedish doctor Lund, (8) has studied experimental gangrene with adrenalin and ergotamine together in rats and has had 100 per cent necrosis in rats which he could prevent by giving adrenalin-blocking agents, such as dibenamine. A protective effect was also observed with local treatment, where nitroglycerine proved to be the most effective. He points out that the venules are particularly susceptible to the vasodilator action of the nitrites.

Meryman If you used a local vasodilator to prevent peripheral vasoconstriction, would not that mean that the blood which was returning to the body from those surfaces would be colder than it would be if the vessels were constricted. In turn, you might get a general, more powerful vasoconstriction resulting from the impact of that cold blood on the central system, so that you might, in a way defeat your purpose?

Adams-Ray That is possible. I have seen quite a lot of people who have been frostbitten before, and they have asked me for advice because when they go out skiing, their feet get numb very very quickly These patients also very often have hyperhidrosis, numbness to cold, and all the sequelae that you see after any cold injury They also have a high vasomotor tone When they go into the cold, they are more liable I think, to get cold injury I advise them to be very careful. I would not put them on military duty in the North. I advise them always to be well nourished, well clothed, and if it is very cold to take some vasodilating agent such as priscoline in the morning and not a drink of bourbon. They tell me that has worked very well, that they have been able to ski.

On my suggestion the Anglo-Scandinavian Arctic Expedition have used a Swedish vasodilating agent, vasodil, as a prophylactic in bitter cold. According to reports that I have just received, they have been very pleased with it.

Burch I would like to raise a question concerning the concept that the circulation to an area remains interrupted by active vasoconstriction to the extent that the vessels kill themselves. Sir Thom

Lewis indicated, when discussing the vasomotor factor in Raynaud's disease, that from a purely hypothetical basis, it would be paradoxical for a vessel to remain constricted to the extent of destroying the tissues in an area without the smooth muscle in the vessel destroying itself that is, if the vessel responsible for the constriction is located in the infarcted area. For smooth muscle to constrict, it would have to have nourishment of its own, and when it becomes *devoid of a supply of blood, it would relax, and relaxation would* likely occur before the tissues could suffer appreciably from a lack of blood supply The only manner in which I could envision the difficulty you describe would be for the vasoconstriction to occur at a relatively long distance proximal to the ischemic area.

Shumacker That happens clinically George. I have seen a number of cases of segmental arterial spasm, including cases of spasm of the femoral artery leading to gangrene of the toes and a portion of the foot. That it was spasm which was responsible and not thrombosis was demonstrated in at least two of these patients by the fact that full return of circulation through the main arterial pathways was subsequently re-established. The period of ischemia may last long enough to produce tissue damage distally even if the spasm is subsequently released.

Burch I do not deny that such occurs. The only way it could happen is, as you indicated, that the spasm is very high or proximal, with a loss of blood supply far distally I am not convinced that there are data available that irrefutably establish such an idea. I have read about those things and I have seen patients who were supposed to have had such a syndrome but I have wondered about the mechanism. *Because it is a plausible concept does not establish* it as the mechanism. How long can the smooth muscle in vessels undergo spasmodic contraction? Do you know Dr Burton?

Burton Well, of course we know that patients with Raynaud's disease do get gangrene. I wonder if Dr Adams-Ray wants us to talk about the protective mechanism of the peripheral tissues, particularly Sir Thomas Lewis hunting reaction which Otto Edholm and Greenfield and his co-workers (9) have studied so much lately I spent some time recently with Carlson and I had his paper to read before it was published, and he makes a very interesting observation there on men who had been bivouacking out in the cold. He finds, on the first day as is apparently normal, that they show this reaction. Vasoconstriction does not persist with

cold, apparently It is broken into by this big swing of vasodilatation periodically But day after day as you expose them to cold, this hunting reaction becomes less evident, so that when they are fully acclimatized, their peripheral tissues stay at a high temperature. The peripheral circulation apparently never gets to the same level of constriction and, instead of having this periodic constriction and dilatation they are now continuously fairly well dilated and warm. But weren t you in your remarks ignoring the existence of this normal physiological mechanism of protection of the tissues? Physiological vasoconstriction, I doubt, ever persists to damage the tissue since before that happens, this reflex, if you like this reaction on the local tissues, supervenes and one has the protective dilatation. One must admit, of course, that in Raynaud's disease and thrombosis and so on, one gets damage of tissue from ischemia, but physiologically it seems to me that the small blood vessels have a protective mechanism against the physiological vasoconstriction.

Siple Most of that is based on rather short term experiments, is it not? When you compare that with the trench-foot damages, does this same mechanism keep on working?

Burton These men were bivouacked six weeks in the cold. I am speaking about Carlson s experiments. Which experiments do you mean, Paul?

Siple I was thinking in terms of the hunting reaction that would affect the constriction by periodic readjustments. In the case of trench foot, it appears that extreme constriction of the limbs is maintained over a period of time Usually within 72 hours you begin to get necrotic effects.

Burton Well, I think in that case the temperature probably is not cold enough, or the temperature gradients are not right to produce this hunting reaction, for which I have a theory I think probably the hunting reaction this has not been investigated, does not occur in the conditions which give trench foot.

Siple: If I might anticipate your theory does it have anything to do with the fact that the pain sensations are not triggered off as a warning under exposure to trench-foot circumstances? There is apparently not a sufficiently sharp gradient of temperature through the skin to set off the pain mechanism. This physiological discrepancy in our warning system occurs when the tissue has cooled down very slowly almost subtly Intolerable pain does not occur when the skin temperature is lowered gradually as compared to the intense pain experienced when the skin temperature is brought down swiftly One of the obvious results, as a consequence is that

in most really cold areas such as the polar regions, trench foot is almost unknown, whereas in the cool temperature regions just above freezing, usually around 40 F trench foot is a very prevalent hazard.

Burton I think the matter is a very complicated one, and there is good evidence, and theory too to show that extremely cold tissue gets along much better than tissue at intermediate temperature. It is the matter obviously of the demand for oxygen and the supply of oxygen. These two things change with the temperature in a different way· one may get very complicated effects. There is a region between perhaps 5 C. and 12 C. where tissue is more susceptible to damage than tissue that is colder Perhaps you would agree that that is a possibility Dr Adams Ray and there is some evidence for it?

Adams Ray Dr Burch, you were referring to the work of Sir Thomas Lewis because he talks about vasoconstriction killing tissue and he believes that the epithelium of the blood vessels is damaged by anoxia, which produces a thrombosis, and so on.

Burch That is secondary In Raynaud's disease, there may be episodes of spasm first then, with impairment of the circulation, local vessel damage, with proliferative changes, occurs. Mechanical obstruction, in turn, permits prolonged ischemia and then damage. The role of the vasospasm in Raynaud s disease is not clear Now whether Lewis was right or wrong, I do not know I only present the concept for comment.

Adams Ray Dr Lund tried heparin treatment to prevent thrombosis, or to see if he could prevent necrosis in these experiments on rats. He couldn t do it with heparin. We all know that tissue can die at temperatures from 15 C. to 0 C., with trench foot certainly I think it is very common. In my own experience, which is not too great, I have seen freezing of the tissue very very seldom.

Burch Is that vascular?

Adams Ray I don t know I should like to discuss that as a combination of cold plus anoxia, followed by constriction, possibly I don t think the hunting reaction totally prevents it, if you have a chap with a high vasomotor tone.

Burton When you said that somebody had shown necrosis induced by adrenalin and ergotamine did you mean the two together?

Adams Ray Yes, the two together

Burton Well, I would be very interested to know whether one could produce necrosis by adrenalin alone, because it seems to me that the peripheral tissues also have a protective mechanism against

continued spasm by adrenalin. We have tried that in perfused preparations, and one gets a rhythmic spasm, because as soon as you stop the circulation, the destruction of adrenalin by the amine oxidase has a chance to catch up. There is no more supply and therefore one finds that the vessels dilate again. I would be very interested to know whether the physiological agent alone, adrenalin, could produce necrosis by spasm.

Horvath Well, it does. You can inject epinephrine subcutaneously and get a nice area of necrosis. Not only that, but if you give them dibenamine, that does not prevent it.

Burton If you mean subcutaneous injection of adrenalin that is not a physiologic effect of adrenalin. It is in the wrong place. I was talking about the amine oxidase in the inside walls of blood vessels.

Kark However in patients with pheochromocytoma you don't see necrosis, at least as far as I know

Adams-Ray But if you chill them?

Kark I don't know

Adams-Ray Dr Lund in his book talks about adrenalin alone. With the doses he employed in his experiments he was not able to produce necrosis in rats with adrenalin alone injected into the base of the tail He refers to an experiment by Braun (10) who using a dose of 0.5 mg. of adrenalin plus chilling of the tail, caused some vascular injury but necrosis only in one case

Horvath Is that just injection?

Adams-Ray Yes just injection.

Horvath Well, injection alone couldn't produce necrosis, but injection plus cold could produce necrosis but you do see necrosis in animals and in man just by injecting epinephrine alone without cold.

Burton What sort of injection do you mean, subcutaneous or venous?

Horvath A subcutaneous injection at the base of the tail in the case of these animals. We can inject it in the shoulder and get necrosis in the animal without adding cold.

Burch How much, Steve?

Horvath One-tenth of a milliliter of 1 in 1000

Burch I know asthmatic patients who have received epinephrine injections at frequent intervals of the day for years. I know one man who has received the drug in large quantities for 40 years and he has not obtained any serious local necrosis. He obtains a little atrophy if he uses one area too frequently but no necrosis.

Webster I think there was a medicolegal case in Canada two years ago where the nurse gave the patient adrenalin instead of novocaine and the patient lost his digit.

Burch That is not local, but diffuse I am referring to local.

Adams-Ray Dr Orr are there soldiers included in your material who were in bad shock when you found them with cold injury?

Orr We have not seen shock associated with a cold injury

Crismon Well, have there been any patients who sustained a battle wound in addition to frostbite, and were they injured severely enough so that their total injury consisted of shock produced by the wound, complicated by peripheral cold injury?

Orr: Those are factors that would be hard to evaluate. We have had wounded who developed frostbite but invariably they had sufficient exposure to cold and enough immobilization to account for the cold injury *per se*

Shumacker You had a few patients didn t you, Ken, in which a main arterial stem was interrupted by trauma with frostbite distally?

Orr Yes.

Shumacker And they had very severe frostbite, did they not?

Orr That is right. I might add that last winter we had a patient who sustained a severe shell fragment wound of the upper thigh resulting in a compound fracture. He was wearing insulated boots and did not develop frostbite of the lower extremities but instead developed a fourth-degree injury of both hands. He was immobilized for a period of approximately 12 hours.

Meryman There was also the man whom I saw who had a shell fragment wound which severed the nerve pathways to one leg. He suffered a fourth-degree frostbite on the other leg, but had no injury whatsoever on the side with the nerve block.

Adams-Ray I am back to what you said, Dr Shumacker about these chaps with spasm of the arteries. If by chance you inject nembutal, or some such thing, in an artery instead of in a vein, the patient will get vasospasm that may cause gangrene of the hand. I think, clinically there is evidence that vasoconstriction of an artery can kill tissue peripherally and local injection of ergotamine and adrenalin can kill tissue by vasoconstriction alone. Don t you think so?

Burton Yes, I would admit all that, but my thought was that there are these protective mechanisms operating in such a way that I doubt if local vasoconstriction which is of physiologic origin, can cause necrosis unless there has been spasm of a distal artery

which is due to a different mechanism, or unless there has been some pathological event, such as freezing of the tissue This may not apply to a particular range of wet cold, in which one gets trench foot, but to exposure to dry cold. I doubt if physiological vasoconstriction alone usually can cause necrosis, without this additional pathological event.

Meryman: The physiological defenses must break down if the thermal loss becomes sufficient, otherwise, the tissue would never progress to freezing.

Crismon: At moderate temperature levels associated with immersion foot or trench foot, apparently the dependent position of the injured part is an important aspect of injury The dependent position and immobility may be the cause of the complication of reduced venous flow

Adams-Ray I will discuss that impeded venous flow in a little while. But what about those people who get frostbite under the same conditions and in the same nutritional state as other individuals who do not? Is it because they have an initially higher vasomotor tone not only in the peripheral vessels but also in the big vessels, and that this hypertonia is augmented by cold, and also by the fear experienced during combat. That is not my idea. It has been proposed by Dueuing (11) in Toulouse that those who have a high vascular tone are the chaps who get frostbitten.

Horvath The same chap who gets rheumatoid arthritis sometimes too.

Adams-Ray I don t know- perhaps It is a very important thing to know as far as prophylaxis is concerned. Some people get frost bite more easily if they are tired, or if they are anemic, or if they are afraid.

Horvath George didn t you try that vascular test of Montgomery on some of those frostbitten patients whom you studied after the war?

Burch Yes.

Horvath If I recall correctly there was no relationship at all between injury and this vascular tone. Of course you blamed it partly on the weather in New Orleans, didn t you?

Burch Well, I did not know if it was due to the difference in environmental temperature. Montgomery worked in Philadelphia during the winter when vessels are probably more constricted. We did our studies in New Orleans during the warmer period of the year We could not reproduce Montgomery s results.

Horvath Well, after your results came out, we tried it over again

Webster I think there was a medicolegal case in Canada two years ago, where the nurse gave the patient adrenalin instead of novocaine and the patient lost his digit.

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Burch Well, I did not know if it was due to the difference in environmental temperature. Montgomery worked in Philadelphia during the winter when vessels are probably more constricted. We did our studies in New Orleans during the warmer period of the year We could not reproduce Montgomery s results.

Horvath Well, after your results came out, we tried it over again

Webster I think there was a medicolegal case in Canada two years ago where the nurse gave the patient adrenalin instead of novocaine and the patient lost his digit.

Burch That is not local, but diffuse I am referring to local.

Adams-Ray Dr Orr are there soldiers included in your material who were in bad shock when you found them with cold injury?

Orr We have not seen shock associated with a cold injury

Crismon Well, have there been any patients who sustained a battle wound in addition to frostbite, and were they injured severely enough so that their total injury consisted of shock produced by the wound, complicated by peripheral cold injury?

Orr Those are factors that would be hard to evaluate. We have had wounded who developed frostbite but invariably they had sufficient exposure to cold and enough immobilization to account for the cold injury *per se*

Shumacker You had a few patients didn t you, Ken, in which a main arterial stem was interrupted by trauma with frostbite distally?

Orr Yes.

Shumacker And they had very severe frostbite, did they not?

Orr That is right. I might add that last winter we had a patient who sustained a severe shell fragment wound of the upper thigh resulting in a compound fracture. He was wearing insulated boots and did not develop frostbite of the lower extremities but instead developed a fourth-degree injury of both hands. He was immobilized for a period of approximately 12 hours.

Meryman: There was also the man whom I saw who had a shell fragment wound which severed the nerve pathways to one leg. He suffered a fourth-degree frostbite on the other leg, but had no injury whatsoever on the side with the nerve block.

Adams Ray I am back to what you said, Dr Shumacker about these chaps with spasm of the arteries. If by chance you inject nembutal, or some such thing, in an artery instead of in a vein the patient will get vasospasm that may cause gangrene of the hand. I think, clinically there is evidence that vasoconstriction of an artery can kill tissue peripherally and local injection of ergotamine and adrenalin can kill tissue by vasoconstriction alone. Don t you think so?

Burton Yes, I would admit all that, but my thought was that there are these protective mechanisms operating in such a way that I doubt if local vasoconstriction which is of physiologic origin, can cause necrosis unless there has been spasm of a distal artery

which is due to a different mechanism, or unless there has been some pathological event, such as freezing of the tissue. This may not apply to a particular range of wet cold in which one gets trench foot, but to exposure to dry cold. I doubt if physiological vasoconstriction alone usually can cause necrosis, without this additional pathological event.

Meryman: The physiological defenses must break down if the thermal loss becomes sufficient otherwise the tissue would never progress to freezing.

Crismon: At moderate temperature levels associated with immersion foot or trench foot, apparently the dependent position of the injured part is an important aspect of injury. The dependent position and immobility may be the cause of the complication of reduced venous flow.

Adams-Ray: I will discuss that impeded venous flow in a little while. But what about those people who get frostbite under the same conditions and in the same nutritional state as other individuals who do not? Is it because they have an initially higher vasomotor tone, not only in the peripheral vessels but also in the big vessels and that this hypertonia is augmented by cold, and also by the fear experienced during combat. That is not my idea. It has been proposed by Ducuing (11) in Toulouse that those who have a high vascular tone are the chaps who get frostbitten.

Horvath: The same chap who gets rheumatoid arthritis sometimes too.

Adams-Ray: I don't know, perhaps. It is a very important thing to know as far as prophylaxis is concerned. Some people get frostbite more easily if they are tired, or if they are anemic, or if they are afraid.

Horvath: George didn't you try that vascular test of Montgomery on some of those frostbitten patients whom you studied after the war?

Burch: Yes.

Horvath: If I recall correctly, there was no relationship at all between injury and this vascular tone. Of course, you blamed it partly on the weather in New Orleans, didn't you?

Burch: Well, I did not know if it was due to the difference in environmental temperature. Montgomery worked in Philadelphia during the winter when vessels are probably more constricted. We did our studies in New Orleans during the warmer period of the year. We could not reproduce Montgomery's results.

Horvath: Well, after your results came out, we tried it over again

and, certainly there is evidence that you can show a difference in vascular tone, at least in the patients with rheumatoid arthritis, and differentiate the potential rheumatoid arthritics from other types of patients. We did our work in the winter and that still may be the disposing factor which you observed originally But at least, if I recall correctly in New Orleans anyway you were never able to show any difference in vascular tone in patients who did or did not have frostbite.

Burch Some of the patients had frostbite but they were mainly patients with trench foot.

Talbott: Colonel Orr did you have any evidence in your follow-up studies of the soldiers frostbitten in Korea that there was a difference in reaction between the frostbite patients and the controls?

Orr No We have just concluded this study on our cases which extended over a period of almost two years after injury

Talbott That was a total of how many patients studied?

Orr There were 72 cases of frostbite in the group. The Landis-Gibbon test, hexamethonium, priscoline, intravenous alcohol and sympathetic blocks were used and no differentiation could be made in the vasomotor response of the feet between the controls and the patients In studies performed soon after injury using cold stress, that is, subjecting the patient to a 50 F exposure, we found signs of marked vasomotor lability In our post injury patients that lability is less marked after one year

Adams-Ray Have you been looking at the arterioles? You have been measuring temperature, haven t you?

Orr We were measuring the skin temperature in the toes and skin color changes.

Adams-Ray: But there is a necessity for looking at their venous tone, because the venous tone might be of importance. Didn't you say Dr Crismon, that the impediment to the return of blood is a factor that will give more necrosis?

Crismon In trench foot, yes.

Shumacker Well, of course, complete blocking of venous return will cause gangrene just as effectively as complete blocking of arterial inflow We see this in cases of phlegmasia cerulia dolens, a type of venous *thrombosis in which* the venous return is completely blocked. I believe we have seen five limbs so affected in the past few years. At the time of amputation it was evident that the arterial pathways were patent but the limbs were dead nevertheless.

Webster Don't you feel there is an inflammatory reaction with that as well?

Shumacker: I haven't been impressed with it, but it may be so.

Webster: We never felt that you could get necrosis of a limb by venous obstruction, unless there was an associated lymphatic obstruction as well.

Shumacker: We did not have any definite evidence of lymphatic blockage. It was apparent that all the veins were obstructed and the arteries patent.

Burch: But you did not ligate the inferior vena cava. Ligation of the inferior vena cava does not change the appearance of the legs appreciably.

Shumacker: You are quite right. I am just saying that total thrombotic obstruction of venous return can lead to gangrene.

Burch: No blood will enter the limb; therefore, whether or not it is leaving the limb is purely an academic matter.

Shumacker: No. That is just my point. To have effective circulation blood must get into and out of the limb.

Blair: Dr. Shumacker, have you ever noticed that on some occasions tails of rats appear to develop gangrene apparently secondary to edema rather than to the actual freezing of the tissue? We have seen it happen in rats that we have exposed to cold. The tail remains perfectly pliable throughout the exposure with apparently no actual freezing. After exposure the tail swells very markedly with massive edema and finally develops gangrenous sloughs. As you know, the base of the rat's tail is bound very tightly to the skeleton. We have suggested that the eventual tissue loss is probably due to obstruction of blood supply at that point.

Shumacker: We have not made that observation. I think it is most significant that you have produced tissue necrosis by exposure to cold without actual freezing of tissues. That must happen in humans very, very often, far more often than as the result of actual freezing.

Blair: For that reason we have been rather critical of using the rat's tail as an experimental frostbite site because we feel that the anatomical presence of a very tight binding connective tissue ring at the base of the tail may provide a tourniquet action which, with edema, may interfere with blood supply and produce gangrene. Of course, this is secondary to cold but it is not cold injury *per se*. It is actually an anoxia injury due to edema which might be produced in any one of many ways.

Adams Ray: Were the tails warm or were they cold?

Blair: Oh, the tails were cold, but they remained completely pliable and freely movable. When a rat's tail freezes it is...

as a metal pipe. After these nonfrozen tails have been rewarmed, usually in 24 to 48 hours, the tail swells with massive edema, and near the base of the tail a bottleneck forms about the connective tissue ring to create a pressure tourniquet We think some of the gangrene we get from cold exposure of rats tails may be the result of this tourniquet action disrupting blood supply to the tail, and not a result of direct cold injury to the tissue itself

Adams-Ray There is a point I would like to stress, and it is an observation of Dr Kreyberg (12) in experimental trench foot in animals He saw that when they were exposed for several hours, the arterioles and the venules were constricted. There was no blood coming through the tissue. But after a few hours I can t give you



FIGURE 23. Marked decrease of swelling in the rabbit right leg following subcutaneous injection of 800 TRU of hyaluronidase. Both legs were exposed to −57°C for 4 minutes. The picture was taken 22 hours after injection of enzyme and 25 hours after injury

the exact number of hours, there was a hunting reaction. The arterioles opened up somewhat but the veins were still constricted, and then there was edema. He thinks that part of this edema that you speak about, Col. Blair might be due to the vasoconstriction of the venous side being stronger than that of the arterial side

Webster: We did some experiments this winter on the effect of hyaluronidase in absorbing the edema and the role that it might play in the extent of gangrene (13) Both hind legs of rabbits were exposed for 4 minutes at a temperature of –35 C. to –37 C. Three hundred turbidity-reducing units (TRU) of hyaluronidase were injected subcutaneously into the edematous tissues of one leg 3 hours and again 27 hours after exposure The changes in volume of the extremities were determined by measuring the amount of water displaced during immersion of each extremity Figure 23 shows the rabbit's extremities 22 hours after injection of hyaluronidase into the right leg where there was marked decrease in swelling compared with the control left leg which presented extensive edema. Figure 24 shows the volumetric curve of the formation of edema in both the injured and control extremities. We found no diminution

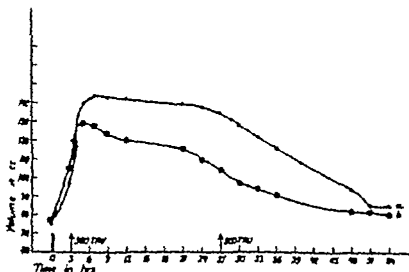


FIGURE 24. Volume changes in rabbits' legs after exposure to –37 C for 4 minutes. The lines indicate the mean values in 6 extremities (a) in the controls and (b) in those treated with hyaluronidase. Reprinted, by permission, from Pirozynski, W. J. and Webster, D. R. Effect of hyaluronidase on edema following experimental cold injury. *Proc. Soc. Exper. Biol. & Med.* 80, 305 (1952).

of the gangrene. The amount and onset of gangrene was almost identical in the two extremities in this series indicating that tissue necrosis is not primarily related to accumulation of edema in the region of cold injury

Horvath In actual freezing experiments and we have not had those interesting experiences you just recounted, I have not been impressed with the fact that the edema was so massive as to occlude circulation to the tail of the rat. With reference to Dr Burch's comment about local or proximal vasoconstriction, I do think we have evidence that where you have a severe cold injury to the distal portion of an extremity you do have intense vasoconstriction of major arterial stems proximal to it. We obtained some such evidence from arteriographic studies, and, estimating the size of the main arterial pathways in both lower extremities after having frozen one it was pretty apparent that there is a good bit of proximal vasoconstriction as well as local vasoconstriction.

Adams-Ray That has been shown by Leriche (14) too.

Horvath I think those observations of Dr Webster's are really very significant to all of us I think we are ignoring the fact that here we have an instance where edema was definitely reduced to an appreciable extent, and still necrosis and the residual changes following cold injury proceeded as expected. That certainly does not seem to correlate with the other comments that edema is the primary thing.

Meryman We have been talking about two different things haven't we? Dr Webster has been referring to a freezing experiment in which there has been a very severe mechanical damage by ice crystal formation which in itself is perfectly capable of causing tissue necrosis. Some of this other work refers to injury from temperatures above freezing which causes vasoconstriction and, I think, anoxia, in which the edema may be one of the mechanisms by which anoxia is produced.

Horvath But you have no evidence that in these rats exposed to an identical situation, the rat tail in one case did freeze and in the other case it did not happen to freeze or that there aren't a number of ice crystals formed in there some place which may not be enough for you to notice but which cause damage in the same way Ice crystals may result and be the cause of the edema initially

Blair Another possibility is the difference in techniques that are used to produce cold injury Dr Shumacker's technique I think, was by circulating fluid through a test-tube arrangement about the

rat's tail. How long were they exposed to cold and at what temperatures, Dr Shumacker?

Shumacker I don't remember at the moment, but in the earlier experiments the freezing was inflicted by a brief period of immersion of the tail in a freezing mixture (15 16)

Blair That's right, direct immersion. And the later ones?

Shumacker The later experiments were carried out by exposing the unanesthetized animal to a low environmental temperature for a longer period of time (17)

Blair Where the exposure may have been a matter of 15 or 30 minutes immersion as a means of freezing --

Shumacker It is much shorter than that.

Blair It is a different type of cold stress from ours where there is exposure to a low ambient temperature for eight hours to produce the cold injury In the later case you have eight hours of prolonged vasoconstriction producing cold injury which may be quite different from that produced by immersion for a few minutes in a fluid.

Shumacker I have the feeling that one might have to look for the explanation of the gangrene resulting from a nonfreezing injury to the rat's tail during exposure to a low ambient temperature in damage to the blood vessels or direct injury from cold rather than in edema *per se* I may be quite wrong, but we see massive edema in human beings from various causes and we don't see gangrene provided there is no occlusion of arteries or near-total occlusion of veins. In elephantiasis a limb may be many times normal size and the edema lasts not for a few hours but for years and years and tissue necrosis does not develop.

Blair Yes. The point which has caused us some concern is that we have observed the tails of rats remain flexible throughout cold exposure later develop edema, and finally gangrene We have never experienced this phenomenon in the feet or ears of rabbits and rats. The only explanation we have is that in feet and ears this tight connective tissue ring does not exist. Thus frostbite edema of the ears and feet does not disrupt the blood supply to the extent that it does in the rat's tail Maybe this is a false explanation but it is the only difference of which we are aware

Shumacker But we see many patients who have not had any actual freezing of tissues in whom tissue necrosis develops.

Blair Oh, yes, you do in trench foot.

Shumacker Well, we do in frostbite also. The majority of the cases studied by Dr Adams-Ray during that severe winter in Stockholm, for example had no evidence of actual freezing (18).

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Shumacker Well, we do in frostbite also The majority of the cases studied by Dr Adams-Ray during that severe winter in Stockholm, for example, had no evidence of actual freez-

the same as that of normal skin and no significant differences were noted in the gain of tensile strength as compared with that of the control incisions. Dr Lempke and I tried to isolate and freeze other tissues. When a segment of the isolated sciatic nerve was frozen solidly we did not observe return of function. It is possible, of course that a different outcome would have prevailed if a different technique had been used, for example, more rapid freezing followed by rapid rewarming. Certainly the frozen skin survives and appears to be capable of relatively normal healing.

Adams Ray How was the repair of the frozen skin studied? That would be interesting. Did you make an amputation or did you study that histologically?

Shumacker We didn t study them histologically

Adams-Ray If you ask a man with trauma (cold injury included) of one hand to show you both hands you will see, that the whole hand with the trauma is paler than the other one in about 40 per cent (Figure 25) Sometimes you have only a pale zone surrounding the trauma and, as in bacterial infections, you may see the red zone surrounded by a pale zone. If you have a paronychia, you may have a red zone on the dorsal surface of the finger and on the volar side an intense paleness. You see the same thing if you have a tenosynovitis. You will see that the skin over it is not red, but pale.

This pale reaction of the skin can be measured with a photometer as suggested by Dr Niels Jarløv in Copenhagen (Figure 26) A light of 5500 Å is thrown on the skin, at this wavelength there is a maximum absorption for hemoglobin. If the skin is red, it will absorb more and reflect less than a pale skin. The reflexion is measured by the photoelement. We measured the normal variations between identical points on the hands, and so we have been able to see if there is any difference in color of the skin. In about 90 per cent of all the cases, you can thus show a pale reaction on about the second day after the trauma. It will extend and its curve will go upwards and reach its maximum after about one day and then it will gradually pass off If you have only a cut wound, it will be gone after a week. If you have a fracture, it will stay much longer

You may ask, what does pallor imply? Wetzel and Zotterman (19) who were working with Sir Thomas Lewis, studied which vessels gave the red color to the skin. When compressing the skin with a glass slide they found that at the instant the skin paled, the capillaries were still open but the venules which belong to the subpapillary venous plexus were flattened out. Pallor is thus a sign of diminished state of filling principally of the venules.

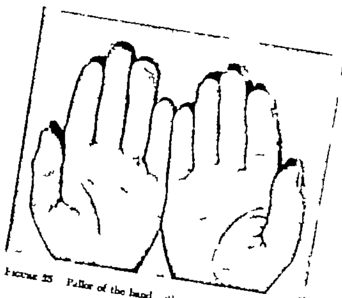


FIGURE 25 Pallor of the hand with paronychia of one finger

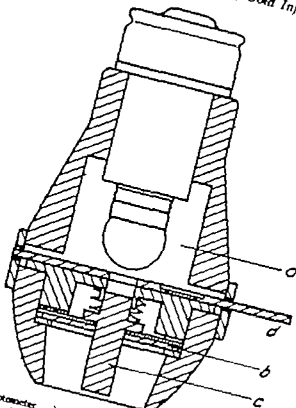


FIGURE 28. Photometer) source of light, b) selen-photoelement,) rod of plexiglass, d) filter holder (5500 Å and 7000 Å)

Pallor might be due to compression by edema. But you can see it without any signs of edema and when I studied patients with pallor and edema the maximum of pallor didn't coincide with the maximum of edema. Pallor must thus be due to an increased tone principally of the venules.

Infiltrating the triggerpoint by blocking the afferent nerves or the sympathetic ganglia directly or intravenously by hexamethonium can abolish the pallor temporarily. Pallor is thus a reflex hypertonus in the venules mediated by the sympathetic (20,21,22,23).

Burton Dr Adams-Ray did you know that if you used cross-polarized light and a green filter you increased the contrast very much more (24)?

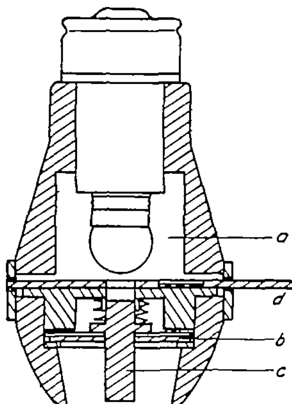


FIGURE 20. Photometer) source of light, b) selen-photoelement,) rod of plexiglass, d) filter holder (5500 Å and 7000 Å)

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FIGURE 23. Case of acute cholecystitis showing segmental blanching in area with artificial hyperemia (ultra violet light)

a distended bladder in this area (29) The venular constriction reactions are thus not only a local response to trauma, but there are also viscero-cutaneous reflexes of the same type often there is a very great intensity of the pallor

I think there might be something of interest, pathophysiologically in this high tone in the off-flow system. Sir Thomas Lewis (30) showed several years ago that the venules can contract with very great power so that they can resist a pressure of up to 100 mm. of Hg. A high tone in the venules might thus theoretically produce slowing of the blood stream with more blood sludging, augment the filtration of fluid into the tissues and diminish reabsorption on the venous side of the capillaries and thus give more edema. I think that the high tone in the venules is one of the factors giving rise to stasis and edema, important factors not only in cold injury but also

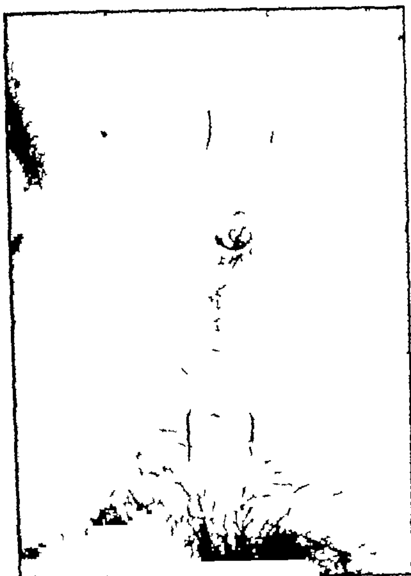


FIGURE 79 Normal subject with descended bladder showing blanching within dorsal segments 11 12. Artificial Hyperemia, produced by mustard oil solution, within the black lines.

in general pathology I wanted to know if I could show that in some way and then I thought of looking into the traumatic edema, which we know can be diminished by sympathetic blocking. My impression is that the effect comes very quickly sometimes before the patient says, My hand is warm.

Shumacker Another thing, Dr Adams-Ray with which I am sure you are as impressed as I am is the observation of good filling of the superficial veins of the hand or foot immediately following an effective regional sympathetic procaine block. This phenomenon so regularly follows sympathetic block before the limb becomes warm and dry that we have learned to take its occurrence as evidence that the injection has been successful in anesthetizing the sympathetic chain.

Adams-Ray That is very nice to hear because I think some of the action of the blocking of edema is due to releasing the high tone of the off-flow side, because in some of these patients, you have a hand that is warm, the arterioles are dilated up to maximum and still you have an effect on the edema.

Shumacker That is right.

Adams-Ray Well, I wanted to investigate this effect of blocking, that has always seemed to be somewhat mysterious. Dr Leriche (14) who initiated the treatment of traumatic edema with sympathetic blocking says, "I don t understand how it is that when I have arterial dilatation and block I still have an effect. I can t explain it, but the fact is there. When I wanted to study volume differences I was a little afraid of plethysmographs, so I went to Professor Hallert at the Photogrammetrical Department of the Royal Institute of Technology with my problem. Photogrammetry is a very good way of measuring, and I would like to say something about it. I think you might have quite some interest in it.

Talbott Yes, of course.

Adams-Ray You all know from your stereopticons that if you photograph an object stereoscopically you can reproduce it as an *optique modele* If you put the two photographic plates in an apparatus called a stereocomparator in front of two light projectors, you can put a point-index on identical places on the plates (m_1 m_2) These points will then unite in one model-point (M) (Figure 30) If one of these points is displaced laterally the point M will move in a vertical direction. This lateral displacement can be read with a mean error of 0.001 mm. In the stereocomparator you can in such a way move the point M in several directions and measure very accurately

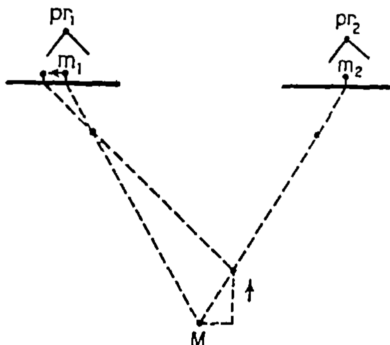


FIGURE 30. pr and pr = light projectors.

Using this technique as shown in Figure 31 the finger is stereophotographed simultaneously from both sides without any pressure on it whatsoever The diameter is computed from measurements from the metal plates to the dorsal surface and from the other pair of stereographs to the volar surface. The mean error when examining a metal piece of known dimensions was 0.06 mm. The mean error when examining a finger on different occasions with an exposure time from 8 to 10 milliseconds was 0.1 mm. (error of the method + normal volume-variations)

Patients with traumatic edema were blocked intravenously with hexamethonium and the volume changes of both the swollen and the corresponding nontraumatized finger were measured. The preliminary results (31) showed an augmentation of the volume in the latter which was due to vasodilatation and which has been observed by other authors. At the same time the volume of the swollen finger diminished. This seems to me to show that the off-flow from the nontraumatized finger became greater than the in-flow that the sympathetic blocking diminished the augmented tones on the off flow side of the circulation.

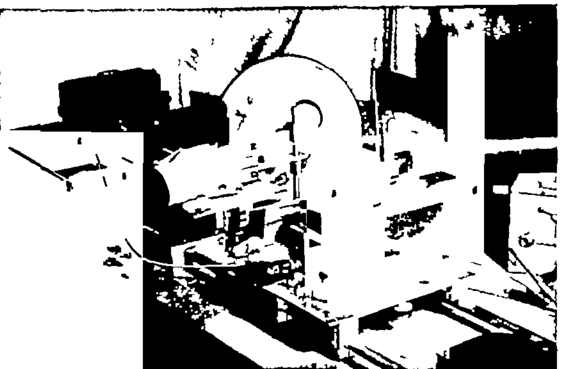


FIGURE 31 Photogrammetric measurement of volume changes of fingers.

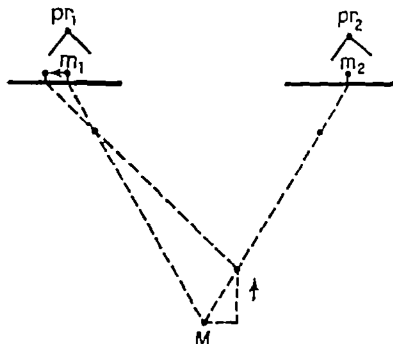


FIGURE 30. pr_1 and pr_2 = light projectors.

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FIGURE 21 Photogrammetric measurement of volume changes of fingers

FIGURE 82. Photogrammetric measurement of swelling of cheek after extraction of the eighth molar. Reprinted, by permission, from Bjorn, H., and Lundqvist, C.: A photogrammetric method of measuring the volume of facial swelling. *Oral Surg.* (In press)

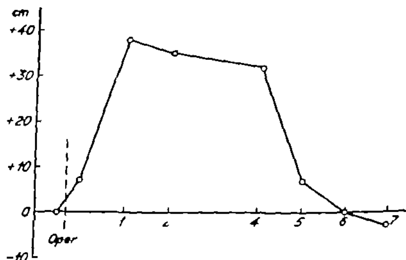


FIGURE 83. Swelling of cheek after extraction of eighth molar. Reprinted, by permission, from Bjorn, H., and Lundqvist, C. A photogrammetric method of measuring the volume of facial swelling. *Oral Surg.* (In press)

Professor Björn and Dr Lundquist (32) at the Dentistry School in Malmö, measured the swelling of the cheek after extraction of the eighth molar by the method demonstrated in Figures 82 and 33. The mean error of this method of measuring the swelling of the cheek in clinical material is 1 7 ml. My curves from fingers followed a similar course with the swelling normally passing away rather quickly (Figure 34)

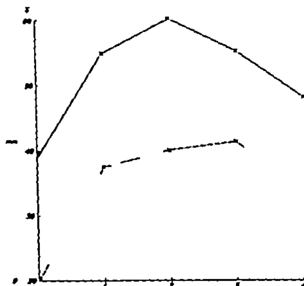


FIGURE 34. Pallor and edema after clean cut wounds of finger
— pallor
edema

In some cases though, after cold injury and after other trauma, the edema will not pass away It will organize it, it will stiffen the joints it will disturb the patient very much. In the first period after the trauma, you can expect biochemical agents to be liberated or formed in the wound or in the frozen tissue, but when you come to the second week, third week, or fifth week, when everything ought to be resorbed, why is there a steady outpouring of edema? Why have you got vascular reactions that go on? Why do the patients have pain and hyperalgesia?

Granit, Leksell and Skoglund in Stockholm (83) have shown, by a very nicely done neurophysiological experiment, that if you cut a nerve you will have a fiber interaction, the motor impul

passing over into the sensory nerves. As you always have some motor impulses going on, you will have a steady inflow of sensory impulses giving rise to different reflexes to cause pain and vasomotor disturbances which can account for the persistence of edema. Dr Granit has told me that he can show the same thing if he has a nerve with a regeneration-cone. It is possible that such fiber interaction in microscopical or macroscopical amputation neuroma explains these disabling post freezing and post-traumatic syndromes. The other day I had a patient with an amputation neuroma and a pale hand with edema. When I pressed on the neuroma her hand paled still more as could be seen when I measured its color Hence when I gave her an increase of sensory impulses, there was a reflex with vasoconstriction of the venous side.

Thus when you talk about the vasoconstricting effects of cold and the vasoconstricting and vasodilating reactions after cold, you must not think only about the arterial side. Sometimes you have vasoconstriction effects also on the arterial side after thawing as has been pointed out by a German scientist, Schneider (34) You must also think of the off flow side of the circulation, especially as stasis seems to augment necrosis. I don t think that high tone on the venous side is the only thing giving stasis because there are lots of other things giving it. I am quite sure that it is one of the factors.

Talbott I would like to have Dr Burton tell us about the venous reflex that he has been interested in.

Burton: This has just been published (35) It may have some relevance perhaps not directly to the sequelae of frostbite, but certainly it is well to know that there is evidence now we think, that there is a local reflex, such that whenever one distends veins in a limb this causes a great decrease in flow in that limb. One only has to fill the veins in a limb to obtain this evidence of vasoconstriction. Whether it is the veins that are getting smaller due to this reflex activity or whether it is the arterioles, I don t believe we can be sure I myself think it is the arterioles.

We first got a clue about this from animal experiments that Dr Girling was doing in my laboratory when he was measuring what we call the "critical closing pressure in the leg of a rabbit. He did a double cannulation of the femoral artery with plastic cannulae, interrupting the femoral artery by a loop. There was a side tube that went to a manometer system through a bag, and thus measured the pressure in the femoral artery All other vessels, other than the femoral artery and vein, were clamped off Then, when the arterial side of the loop was temporarily clamped, the leg got its supply

1 from the pressure in the manometer and the manometer pressure came down as blood flowed through the leg. But what we have been studying for some years is that it does not come down to the bottom, but stops at what we call the critical closing pressure," which we think is a measure of the vasomotor tone and the tension in the walls, probably of the arterioles

Dr Girling measured the venous pressure at the same time in this experiment. It also fell but was considerably below the point where the arterial pressure stopped. Well, that was fine, but I told him that it would be interesting if he were to raise the venous pressure in this experiment. If one should reach a point where the venous pressure was artificially raised above this critical closing pressure then the arterial pressure should stop at the venous pressure. The two final pressures should be equal. He tried that experiment, and found that as you raise the venous pressure, the arterial critical closing pressure goes up too, so it is always above the venous pressure (36) This is true unless you give some more anesthetic to the animal so it is deeply anesthetized. It looks as though there must be some back action, that raising the venous pressure somehow changes the critical closing pressure which we are pretty sure is an index of tone more on the arteriolar side

Dr *Gaskell, who is now in England on a fellowship with Professor* Henry Barcroft, worked on the human digits last year We were interested in the effects of posture on flow We worked with a tilt table device, in which we did not tilt the whole body but just lowered one leg and kept the other leg level, to act as the control. We measured the blood flow in the toes by the standard plethysmograph method. Suddenly when venous occlusion is produced by a cuff just behind the plethysmograph which temporarily occludes the veins, there is a rise of the volume in a curve which eventually becomes flat. On release of the venous occlusion the volume comes back to the original base line. This is the standard picture. It has been argued that that initial slope measures the rate of inflow because at that instant you have stopped the outflow but have not yet interfered with the inflow At the top of the curve during occlusion of course, the pressure is piled up in the vein, so that now the blood is slipping past as fast as it is coming in, but the initial slope is supposed to give the undisturbed blood flow

That is the picture everybody finds when the limb is level, but the moment the limb is put down below the horizont d the veins are full, the picture changes. The initial slope le and when you release the occlusion, the curve g o



below the baseline and comes up again. *Evidently when the veins empty* the volume of the finger or the toe is now much less than what you started with. Then there is a subsequent increase in volume. If the vessels have *any considerable vasomotor tone* and are constricted this change in the record goes one stage further. In this case the only effect of blowing up this venous occlusion cup is a shrinkage of the finger. All one did was to dam up the venous return in this finger and yet the result is that the volume of that finger began to decrease. I don't see how you can possibly get any explanation of this other than that there was some reflex, meaning a reaction from one set of vessels acting on another which caused this.

We found that we could get exactly the same pictures if we left the limb level and simply blew up an occlusion cuff which can be quite distant. For instance *if you leave the leg level, meaning* the volume and flow into the toe, and blow up a cuff on the ankle with 20 mm. of mercury pressure, the toe immediately shrinks. It seems to me that you have to say that that rise of venous pressure somehow elicited a reflex effect which caused a vasoconstriction of some kind in the toe. It is a local reflex. It doesn't happen in the other limb and it is still present and just the same in the sympathectomized limb in the patient with a unilateral sympathectomy. We need to do much more. We should find, following up Girling's animal experiment, that under anesthesia, perhaps the local reflex is not present.

As a result of this, we can plot only the apparent blood flow. One must realize a serious import of these experiments that is, when we know about this reflex, the latency of which is extremely slight, one no longer can say that the initial slope will be a true measure of the undisturbed flow. This reflex can affect the curve of volume in the first beat, as soon as the veins are dammed up. My faith in *the classical plethysmographic method is completely* shaken, except in the case where the limb is up and the veins are empty because now I think we can prove that there is always this reflex effect arising from the act of measurement. *Obviously* the initial rate of *increase of volume is the sum of* the blood flowing in, plus the reflex shrinkage of vessels. One can attempt to correct it by taking a line joining the original baseline to the bottom of *the afterdrop* as the baseline instead of a horizontal line, but, obviously the correction is not very good.

However taking these apparent flows, or even the corrected ones, with angles of title of −15 −90 −45° or plus 15° 30° 45

the apparent blood flow into the toe or the finger changes greatly with posture It is maximum at about the horizontal, and falls off very much indeed as you lower the limb On raising the limb, curiously enough, it also falls off but for a completely different reason. Lowering the pressure in vessels by the hydrostatic factor I think, is another way of demonstrating this critical closing pressure. If they have vasomotor tone, the pressure may drop below the critical value, and they close. Normally if you put an arm up to about 60 there is no more flow in the finger That may not persist, of course.

One result really excited us. We wanted to find out if the reflex effect existed after sympathectomy The patient we obtained was a person with a unilateral sympathectomy for Buerger's disease and the blood flow on the unoperated side was extremely low indeed. On the operated side, it was 10 or 15 times as much and in the normal range, so the operation evidently was successful in preventing gangrene After studying the operated side we found that the reflex existed there But we noticed that on the unoperated side, which remained level, the signs of this reflex were very marked indeed, whereas in normals, when you put the arm or the leg level, you don't see the afterdrop which is the sign that this reflex is operating. I am quite convinced, however that even when the limb is level, the reflex is there, although it doesn't show itself in this afterdrop. But in this patient with Buerger's disease the afterdrop was most exaggerated even when the leg was level, and it did not disappear until you put the unoperated leg up to 30 degrees. At this angle, the blood flow in that limb affected with Buerger's disease was just as great as on the operated side

It certainly looks to us as though this particular patient perhaps was suffering from an exaggeration of this normal reflex. His central venous pressure might have been normal, but because of the disease process in his small veins, his local venous pressure must have been high A Buerger's disease patient must obviously have a bigger gradient of pressure than normal to provide the venous return This reflex might cause the vasoconstriction in his digits, which led to the ischemia.

Now does this sort of reflex fit into the physiological picture? I think it does very well, because, as you know the discovery of the carotid sinus mechanism for dealing with postural changes, causing a vasoconstriction in the dependent limbs to keep up the blood pressure was very satisfactory and very satisfying to all of us I don't know that we stopped to think whether or not this could

do the complete job that is needed. After all, you have to have a change of central blood pressure to elicit the carotid sinus reflex and the effector mechanism via the sympathetic is completely diffuse and *en masse* The sympathetic nervous system always affects both limbs and thus the carotid sinus mechanism cannot look after possible vasomotor changes in cases where one leg is up and the other leg is down. We have no knowledge of the mechanism but we are sure that there is this mechanism in the vessels of the limb by which a distention on the venous side does produce a very great diminution of flow and a vasoconstriction.

I know this will arouse a lot of argument, but we don t see another explanation. The application to this conference in terms of frostbite, is that this factor may be operating, maintaining a vasoconstriction during recovery It might be worth trying to see what happens if the limbs are elevated to drain the veins. Whether or not the sequelae of frostbite do include an exaggeration of this reflex, I don t know As you see, it doesn t quite fit what Dr Adams-Ray has been telling us or has been discussing, but I think it is relevant, perhaps, in another way to the problem.

Crismon Dr Burton, I would like to comment that this experiment is reminiscent of work, reported by Brun (37) some years ago from Copenhagen, on observations of vessels in the rat stomach. In his experiments, the procedure differed considerably He was measuring the diameter of arterioles under microscopic examination. He found that when ephedrine was introduced into the animal, he could measure the constriction of arterioles, as one might expect. However if those vessels were provided with some sort of isolation in the form of a local anesthetic, applied in a ring around the area of observation so that all the vessels coming into the region were at least in contact with this local anesthetic, then he found that intravenous injections of ephedrine caused, not a constriction of the arterioles, but a dilatation The only vessels that closed under those circumstances were the capillaries.

I wonder if perhaps your interpretation of the phenomenon, depending upon the venous trigger might possibly be modified to one that would extend to a trigger that might lie anywhere downstream from the arterioles, since the impulse for vasoconstriction under these circumstances appears to be the distention of the arterioles and not the action of ephedrine directly on their walls.

Burton I think we have to admit that we can t say definitely where the trigger is, nor can we be absolutely sure that it is the arterioles which are closing off rather than the venules. My feeling

is that the changes of flow which one gets are so dramatic that I doubt if a change of venous resistance, which after all, is not a very major factor of the total resistance could account for them. I am inclined to feel that the motor part of this reaction must be in the arterioles but the trigger part of it, I would admit, could be from the venules or the capillaries.

I should explain that when Dr Gaskell told Dr Henry Barcroft about this, the latter made an excellent suggestion that has to be considered that is that this could be a sort of myogenic reflex of the veins themselves. This has been talked about many years ago. When one fills a vein, somehow or another the vein manages to react so that it gets smaller This seems a most complicated and paradoxical sort of thing to me, and I have never seen the superficial veins when one dams the blood back, do anything but get bigger Dr Barcroft also said that the after drop in the records could be simply because you have filled up a vein during the experiment, that these veins now have a large tone, which when you release the occlusion persists for a little while. This would give an overshoot in the volume upon release of the occlusion, followed by recovery Of course, this could explain the afterdrop, but it could not explain the experiment in which the flow is very small when the limb is level. When the man is cold, when the limb is down, the only thing that happens is that the volume decreases during the occlusion. It couldn't explain that, could it?

There is a possibility that there is some direct reaction of the venules, and that somehow or another they have a myogenic reaction so that when you raise the pressure in them, they respond by getting smaller But as a biophysicist, that does not appeal to me. Wouldn't it require a very complicated sort of mechanism? It would be very paradoxical, wouldn't it? It is not very acceptable to me. I prefer to think that possibly there are baroreceptors in the veins, or possibly in the venules, which are connected by some nerve plexus to the vasomotor side. I think we ought to think of the carotid sinus baroreceptors as just a specialized case of baroreceptors all over the vascular system, which, as you know are being found in a variety of places now

Burch I do not know if Dr Burton has seen our old papers. When I was working with Dr Turner and Dr Sodeman, we published (88) the phenomenon of variations in pulsations with variations in position of the limb with respect to the level of the heart. We found essentially what Dr Burton has. We could vary the level of the fingers 10 cm. above or below the level of the heart and

could not detect any change in the volume of pulsations of the finger tips. Above or below that level, they changed. We suggested that an increase in venous tone was partly responsible in pulse volume when the part was below the level of the heart.

Then we observed essentially the same reactions in the veins in the finger tips of a man held at heart level which Dr Burton described (39) We noted the same overshoot. We attempted to quantitate the pressures and volume changes involved in the responses It was our opinion that the changes occurred in vessels distal to the arteriolar side because of the large volumes involved. We employed such responses as a measurement of what we called, "venous tone" or "vascular bed tone, other than arteriolar We studied several patients with acrocyanosis a disease in which the veins are supposed to be partly or greatly at fault and found this rebound phenomenon absent. A certain number of the patients had definite changes from the normal.

We searched for an optimal pressure required to produce the reaction. It was found that there was a critical occluding pressure. If high pressures are employed, the response was not noted or different

Up to the present time, we have never measured blood flow by the venous occlusive technique, using the plethysmograph, although we have been interested in plethysmography However we did not measure the rate of blood flow because of obvious difficulties with the technique. Within the last few months, I have been interested in reinvestigating some of these problems involved in venous occlusive techniques for measuring blood flow Dr R. H. Turner initiated these studies at Tulane University School of Medicine but never reported his results Previously reported measurements of blood flow by the venous-occlusive technique should be accepted with considerable caution.

Burton I am afraid so I would have preferred this to every other method. I always felt it was something that gave you milliliters per minute directly without argument about calibrations, and which was really measuring what you wanted to know It was so much better than the dozens of other ways by which you can measure something related to blood flow But I am now forced to feel that unless I am sure the veins are empty I have to regard the initial slopes that one measures with suspicion.

Adams Ray Yes, and if you begin the tests and the veins are constricted, that will give you a very flat curve. Dr Edholm said at the conference last year that when venous occlusion is applied,

when speaking of the effect of cold on the venous circulation there is an immediate rise in volume of perhaps one pulse beat alone, and then the volume record flattens off That implies that the venous reservoir is very small or very inelastic. I should say it is because the veins are constricted.

Burton It might simply be that they are full.

Burch Yes.

Burton I visited Greenfield in Ireland two years ago, and he told me he was looking for this hunting reaction in fingers. By the colorimetric method, with the finger in a Dewar flask, he would find the heat given off decreased in the cold and, all of a sudden, went up to high values But when he was taking records with a plethysmograph at the same time, he could find no trace of any increased flow at this moment. When I looked at his records, it was obvious that upon occlusion the curve of volume increase went flat very very quickly within one beat. His recording system was not a fast response system, so that one could not hope to analyze beat by beat, as Dr Burch does, and still approximate for this initial slope. Apparently the plethysmographic method therefore is of no application when the venous reservoir is so very small.

Adams Ray We have something like it in the clinic, when there is irritation of a vein. You have venous constriction with thrombophlebitis or phlebothrombosis as has been pointed out by Ochsner (40) and Leriche (14) But some times when you have a deep thrombosis of a vein, you have a reflex constriction on the arterial side too

Burton I have always taken that as encouragement to think that there are reflexes which are elicited from the veins which affect the vasomotor side.

Burch An experiment we did last week might throw further light on what Dr Burton was talking about. While studying the plethysmographic method of measuring blood flow in a subject we have studied several times under various physiologic conditions we noted that his rate of flow was greater at a comfortable room temperature than at a hot and humid one. This was due to an error in the method and not necessarily to the fact that the rate of flow was less in the finger tip in the hot room. Apparently the veins of the venous reservoir in which the blood is trapped when the veins are occluded were too full to hold the blood rushing into the finger from the arteries, and blood leaked out of the finger under the occluding cuff, resulting in the measurement of an erroneously small rate of blood flow When the room temperature was 12 C., the

rate of flow was measured to be zero. This small value may have been due to an error produced by a tight venous system, too tight to accommodate any blood that might be trapped distal to the occluding cuff as well as to arteriolar constriction produced by the cold. The relative role of each factor has not been evaluated yet.

Burton It might be either. We feel that such low flows would be consistent with the complete vasoconstriction that you start with. The disturbing thing for the plethysmographic method is that you get a marked apparent dilatation, judging from the heat given out by the finger which is more than you ever get even with complete vasodilatation, and yet the plethysmographic method in those circumstances does not show anything.

Burch Of course, and that is due to the shortcomings of the technique.

Burton Does what I have been saying about the possible reaction elicited on the vasomotor side from the veins apply to frostbite? Does one get a blockage of the venules and small veins, let's say by the blood cells in frostbite, so that one could imagine there was a distention of the venules and veins which might elicit this vasomotor reflex? Does anybody know whether one does get mechanical occlusion by packed cells in frostbite of the veins?

Adams Ray I couldn't tell you about frostbite, but Knisely (41) has shown that the blood sludging always begins in the venules.

Orr What do you consider to be the cause of sludging?

Adams Ray One of my colleagues in Stockholm, Dr Thorsén (42), has been doing experimental work on how dextran may cause sludging of blood corpuscles and he has shown, very nicely I think, that high molecular dextran gives a very definite sludging. When low molecular dextran is injected, this sludging goes away. He thinks that the blood sludging is caused by chemical action of the thrombin that is released in a traumatized part of the body. That is his theory.

Meryman There is a definite coating formed on the red cells in sludging. We have recently done some electron microscopy of sludged red cells, and it does not seem to be a specific function of the red cell. It is something which is adsorbed onto the red cell, and there is definitely a coating of some material there.

Adams Ray Yes, that is one of his findings, too. He gets that coating if he gives high molecular dextran or if he gives other high molecular things into the blood stream.

Meryman We also found a very heavy coating with polyvinylpyrrolidone.

Crismon The pseudoagglutination must be partly due to molec-

ular configuration and not entirely a matter of molecular size because if one uses ordinary gelatin with its characteristic long molecule pseudoagglutination is very marked. With gelatins that have been modified by a process of coupling and autoclaving, so that the fragments consist of shorter pieces bound together in cross-hatch fashion, rapid red cell sedimentation is less easy to demonstrate, although the molecular weights of the two samples of gelatin, one modified and the other not, are nearly the same. Wherever pseudoagglutination occurs, it is easily modified by ortho-substituted benzoic acid derivatives, such as salicylate. The same process also applies to the joining of gelatin molecules in the process of gelling. Gelatins that ordinarily would be solid at room temperature can be kept liquid by the addition of salicylates. One explanation of this phenomenon is that it depends upon an alteration of hydrogen bonding properties in the gelatin molecules and presumably also the red cell surface.

Adams Ray That is why perhaps the salicylates have an anti thrombotic effect?

Crismon I don t know whether it has anything to do with that aspect of salicylate action. It may partly explain the dramatic changes in sedimentation rate that are achieved early in rheumatic fever when the doctor thinks the patient is getting much better as a result of salicylate medication. It may be only a matter of the altered chemical properties of the red cells. He could produce the change in sedimentation rate equally well, if instead of administering the salicylate to the patient, he administered it to a sample of the patient s blood in a test tube. This is some work done by Dr George Feigen (43) in our laboratory The observation of reduction of sedimentation rate by salicylates added to blood *in vitro* was first reported by Bendien, Neuberg, and Snapper (44)

Brinkhous In regard to the work of Dr Thorsén suggesting that thrombin is the mediating agent in the agglutination of red cells, we have a little work on that subject. We were more concerned, however with platelet agglutination than with red cell agglutination. It is true that crude thrombin preparations would cause the agglutination phenomenon. On purification of the thrombin by removing a number of the protein impurities agglutination would no longer be produced. I would doubt whether or not it is really through the thrombin-forming mechanism that sludging actually develops.

Meryman There are certainly no fibers observable in the sludge coating, that is, there is certainly no fibrin formation as it is usually recognized in the electron microscope.

Webster Is it like an intercellular cement substance?

Meryman It is just an amorphous material.

Kark Dr Crismon if you add a salicylate to any type of blood with an abnormal sedimentation rate can you restore that to normal?

Crismon I don t know Dr Kark. We haven t had an opportunity to do that. I was talking to Dr Weimer at Fort Knox, and I understand that cold agglutination can be completely reversed by the addition of salicylate.

Kark Including cryoglobulins?

Crismon I don t know whether or not Dr Weimer studied that.

Adams-Ray: Have you tried the inhibiting effect of salicylates with high molecular dextran?

Crismon No the only things we have tried are Knox gelatin, P 20 oxypolygelatin, and the recently prepared modified" Knox gelatin We don t know how the modified gelatin is prepared. Actually we know something about its physical properties, but it may well be quite analogous to oxypolygelatin. It is a coupled and degraded gelatin.

Talbott Dr Hegnauer do you have any remarks that you would like to make?

THE HEART IN ACUTE IMMERSION HYPOTHERMIA

Hegnauer To go off into a totally new field I would like to talk a little bit about the heart in acute, immersion hypothermia. Our conclusion, which still wants direct proof is that human deaths in acute hypothermia, induced without benefit of prior anesthesia, are due to ventricular fibrillation. The bases for this view are mainly our observations on barbitalized dogs subjected to hypothermia by immersion in an iced bath at from 3 to 4 C. After an initial rise, the pulse rate regresses with the temperature so that at temperatures of 17 16 or 15 C. in the heart the pulse rate is 20 per minute or less (45) This applies to the majority of such dogs if they have not been subjected to prior surgery and if they are not burdened with intraventricular catheters.

From these low pulse rates there may be sudden asystole or a further regression to 10 5 or even fewer beats per minute and then asystole or ventricular fibrillation The point of these statements is to emphasize that death in asystole occurs only after the rate and temperature are reduced to very low levels. Sudden asystole does not occur from heart rates of 40 or 50 or more these rates are obtained above 20 C.

There is always a proportion of dogs, probably 20 per cent, that die at the higher temperatures and which prior to death exhibit extrasystolic action. Such deaths invariably have been due to ventricular fibrillation, and with extremely rare exceptions have occurred at temperatures below 25° C. Bigelow and his co-workers in Toronto (46) have had a similar experience, but with an even greater incidence of terminal ventricular fibrillation at or above 20 C. Cardiac abnormalities have been a common observation among most people who have worked in the field of hypothermia, and the question of cause has been raised. Tentative answers have been presented, but little direct experimentation has been done. The most common explanation tendered for the appearance of the abnormalities of rhythm and cardiac failure is that of cardiac hypoxia.

That hypoxia is not a factor under the conditions of our experiments is indicated by the following observations first, respiring the dog artificially either with air or oxygen has no influence on the course of the pulse rate regression or the incidence of extrasystolic action. Second, if an oxygen debt had been accumulating during cooling to 20 C. or less, it might reasonably be supposed that a sudden cessation of all respiration would quickly cause the heart to fail. On the contrary at such temperatures the respiration may be blocked completely and the heart may continue to beat and maintain that blood pressure which is normal for the temperature for as long as 25 minutes. Third, Bigelow has cooled dogs to 20 C and maintained them for from 0.5 to 4.5 hours while measuring oxygen consumption, after which they were rewarmed. There was, during the rewarming period, no evidence that an oxygen debt was being paid off while heart rate and blood pressure returned to normal. Fourth, the measurements of the coronary A V difference made by Penrod (47) and its relation to arterial saturation both at normal temperature and at 20 C. and 17 C. indicate that in spite of the marked leftward shift of the oxygen-dissociation curve which occurs with cooling the heart can extract the same amount of oxygen from a unit of blood at the lower temperatures as at normal. The shift causes a lowering of the oxygen tension of the heart muscle, but since the metabolic rate is reduced to perhaps one-fourth or one-fifth of the normal and the cardiac output is similarly reduced this does not appear to have a deleterious effect. Such dogs could be maintained for 15 minutes on a 2 per cent oxygen mixture. These observations indicate to us that hypoxia is not a contributory factor in hypothermic death, although I too had erred originally

in thinking that what proved to be catheter induced extrasystolic action was probably hypoxic in origin.

From the literature on acutely induced hypothermia in unanesthetized human subjects one learns that auricular fibrillation is common at body temperatures below about 31 C that the pulse rate decreases to 50 or 40 per minute at 27 C., that it may be irregular and suddenly disappear that with few exceptions the lethal body temperature is 25 C. or higher Down to this temperature the hypothermic human resembles the minimally anesthetized, shivering, hypothermic dog except that the human auricle fibrillates and that of the dog does not. Whether anesthesia makes a difference in this respect cannot be stated. It would appear that the terminal temperature for most human subjects is between 25°C. and 27 C as suggested from observations of Holzlöhner (48) who described the terminal cardiac action in the Dachau hypothermia subjects, as determined by palpation of the radial pulse. At or near 25 C. the pulse was from 40 to 50 per minute, and frequently irregular just prior to its complete disappearance. Because no one has published terminal electrocardiographic records, one is not in a position to say exactly what caused the cardiac standstill at that temperature

We have been trying to reconcile this observation with the fact that the pulse of the anesthetized dog usually regresses to an extremely low rate before complete asystole or ventricular fibrillation which occurs at from 16 C to 17 C.

Talbott Do you mean electrocardiograms in dogs or in human beings at terminus?

Hegnauer In human individuals I am thinking now in terms of all the experiments that were done at the Dachau concentration camp.

Horvath And in Russia.

Hegnauer They took some EKG records apparently but none at terminus and they did very little with the records taken because they were distorted by the violent shivering of the subjects. The only description or suggestion that I could find as to the cause of death in these human victims was the statement by Holzlöhner

Nevertheless if we subtract from the picture all EKG records which we have obtained on dogs then the unexplained terminal events appear the same in rabbits, dogs and humans. Warren and his colleagues (49) state that in rapidly induced hypothermia in rabbits death is sudden, and is more frequent than among more slowly cooled rabbits which survive to lower temperatures. I see

little difference between this description and that presented by Holzlöhner except that the latter adds the details of pulse frequency and irregularity. Nor is there a difference from our observations on dogs that die suddenly either during cooling or rewarming. Yet in dogs this kind of death is invariably the consequence of ventricular fibrillation. It has never failed.

Now assuming that extrasystolic action and ventricular fibrillation is the characteristic terminal event in hypothermic man, there appear to be at least two possibilities for development of the ectopic foci first, circulating epinephrine, which must be considerable in unanesthetized animals and humans in a very cold bath and second, temperature gradients within the heart muscle itself.

The existence of temperature gradients in the heart is most probable, almost undoubted. On immersion, blood from the cold skin reaches the right heart first. During rapid rewarming by immersion in a 45 C. bath the warmed blood from the skin again reaches the right heart first. It is a frequent observation that dogs mainly produce extrasystolic action from multiple foci shortly after immersion in a warm bath, and fibrillation sometimes may occur within a few minutes, or at any time until the rectal temperature is back to 25 C. or 26 C. when sinus rhythm is completely restored. This phenomenon, we believe, explains rewarming deaths.

The Dachau subjects and the torpedoed merchant-ship personnel and ditched pilots did not experience the benefit of pre immersion anesthesia. In addition to the autonomic discharge of epinephrine due to the sudden cold there was also that which springs from strong emotion, and the epinephrine release must have been considerable It seemed a possibility that the chilled heart might develop ectopic foci more readily in the presence of circulating epinephrine than in its absence or than in the heart at normal temperature. The failure of our barbitalized dogs to exhibit extrasystolic action more frequently might be related to a direct protection of the heart by the anesthetic or to diminished epinephrine release.

We have begun a series of experiments in which epinephrine injections were made at normal and successive subnormal temperatures during cooling. The injections were made at the rate of 10 gamma per kg. of body weight over a one-minute interval. EKG records were made continuously during the injections and until normal heart action was restored or until ventricular fibrillation developed. In the four experiments which have been done, fibrillation developed in one instance at 28 C., in another at 23 C. and in the remaining ones at temperatures between 23 C and 28 C.

Even at a normal temperature ectopic foci appeared in some instances, but the usual picture was one of vagus slowing with or without a shift of the pacemaker to the A V node. At temperatures below 28 C. ectopic foci developed with increasing frequency lasted for from 1 to 3 minutes and disappeared or precipitated fibrillation.

There appeared to be a temperature range between 34 C. and 28 C in which the heart was less sensitive than at normal temperature and then the heart became more sensitive at temperatures in the mid-twenties.

Talbott How long did it take you to get down to 25° C. 26° C. or 28 C degrees in the dog?

Hegnauer· Down to 26 C. in possibly an hour and a half and down to 20 C in about two hours

Talbott How long does it take to deplete appreciably the adrenalin from the dog? Is that a function of days or hours or minutes? Or is there such a thing as depletion under cold stress?

Hegnauer Well, I don t know that there are any data available on that I don t know how long the adrenal glands can continue to produce adrenalin in an extreme degree of stress. It may be of interest to add here that in rats exposed to a mild degree of cold (0 C.) there is a gradual increase of adrenalin in the adrenals up to a maximum which is maintained during the whole period of exposure to cold (51) See Figure 35.

Burton Have you given adrenolitic agents to a dog before you exposed him to low temperatures to see if it affected the course of the experiment?

Hegnauer I tried epinephrine blockade during the course of experiments in which intraventricular catheters were employed. Someone (50) suggested that the extrasystolic action that occurred with ventricular catheterization was a reflex rather than a direct effect. I did a few experiments with epinephrine blockade using the highly specific adrenergic blocking agent SY 21 (N-ethyl-N 2-chloroethyl-9-fluorenamine HCl — SKF 501) and it has absolutely no effect on the ectopic activity induced by intraventricular catheters. I have not tried adrenergic blockade in connection with these experiments.

Burton In view of your idea, it would be very interesting to see if adrenalin affected it.

Hegnauer· Well, we will do that, if the results of further experiments bear out these first observations.

Adams Ray An adrenolytic affect would, perhaps, have some

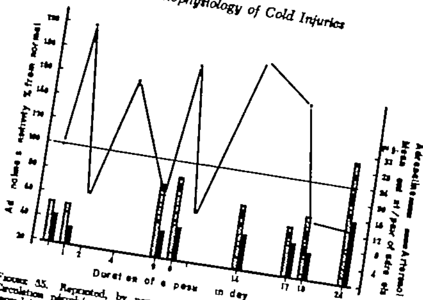


FIGURE 35. Reprinted, by permission, from DesMarais, A., and Dugal, L. P Circulation périphérique et teneur des surrénales en adrénaline et en artérénol (noradrénaline) chez le rat blanc exposé au froid Canad J M Sc 29 90 (1951).

effect on the liver In hypothermia I think there might be a pooling of the blood in the liver in the dog. The hepatic veins of the dog can constrict very strongly In allergic shock, the dog dies because the veins are constricted and there is a pooling of the blood in the liver Thomas (52) makes that statement.

Hegnauer From gross observation we have no evidence that there is pooling of blood in the liver of these animals.

Adams-Ray It is very interesting that there is this association between hypothermia and ventricular fibrillation, because the heart surgeons today want that. Dr Senning (53) working with Crafoord, has just published a thesis on the use of ventricular fibrillation with intracardial operations, with quite a lot of EKG observations There is also a new work on hypothermia by Juvenelle, Lind and Wegelius (54) both of which might interest you

Hegnauer I think there is no question that the heart is more sensitive to ventricular fibrillation in the cold than it is at normal temperatures.

Crismon: Some years ago, we studied the results of epinephrine injection in hypothermic cats We were interested in determining whether or not the rate of destruction of epinephrine was, perhaps, depressed in the cold. In order to do that, we prepared the animals

by sensitizing one nictitating membrane, by removing the superior cervical ganglion, and recorded the constriction of the membrane in the usual way for gauging epinephrine activity. We tested the response of the membrane at various body temperatures. As the animal was cooled, the same dose of epinephrine produced a progressively increasing response in the nictitating membrane. This could be abolished completely by diathermy localized to the liver. The only part of the body effectively warmed was the liver: the temperature of the nictitating membrane measured with thermocouples was demonstrated not to change.

Hegnauer: Diathermy to the liver reduced the sensitivity of the cold nictitating membrane to epinephrine?

Crismon: No, it reduced the response. We don't know anything at all about the sensitivity, but a given dose of epinephrine produced a very much lower excursion of contraction, when the liver was warmed than when the liver was not warmed (55). In some of the animals the experiment was a failure because of ventricular fibrillation after a dose of epinephrine.

Adams Ray: We were told at the conference last year about hemoconcentration and there was a discussion as to where the blood went. Does it go into the tissues? I wonder if the venules and veins don't take part in that hemoconcentration? There are some Swedish physiologists, Sjöstrand, Nissel, and Johnson (56,57,58) who have maintained that the venules in the lungs contract, and pool the blood in the lungs. Glaser (59) found an enlargement of the liver in man during cold and also congestion of the lungs. In dogs, we know that the hepatic venules contract in histamine shock (52). Dr. Ohlson at The Veterinary Faculty of Stockholm and I also found by x-ray a swelling of the liver after laparotomy. Why wouldn't the venules contract when there is hypothermia with circulating epinephrine? To look further into that, we have been doing some experiments on dogs, and I want to describe a method for measuring the changes in volume in a living dog.

Silver indicators of different shapes for identification are placed on the upper side, under surface and free border of the liver of the dog which is then placed on a specially constructed table under two x-ray tubes (Figure 38). When the x-ray tubes are exposed at the same time the location of the indicators can be measured very accurately by an apparatus, which graphs the orthogonal coordinates with the aid of a microscope. The indicators have been placed so that they form a tetrahedron, the volume of which can be computed with an error of five per cent.

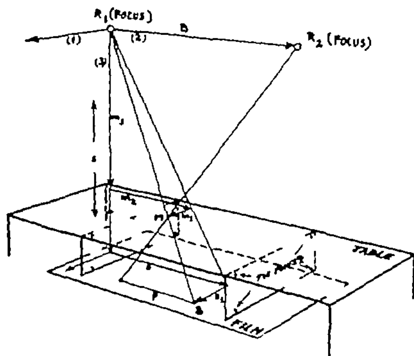


FIGURE 66. Stereophotogrammetric arrangement for localization of indicators, inserted in living tissue.

M = indicator R_1, R_2 = x-ray tubes

The vertical plates of the table each contain four small balls of steel in fixed positions, used to analyze the sources of error. The position of M is determined in the orthogonal coordinate system 1, 2, 3, with the origin at R_1.

In two experiments we have waited several weeks after laparotomy before placing the indicators. We injected vasopressin which is a very strong constrictor especially on the venous side. Before the first dog died in collapse the volume of the liver was measured and was found to have increased by 50 per cent. The second dog received a smaller dose of vasopressin and went into shock with the liver swollen. When he was given an injection of hexamethonium his blood pressure came up and the volume of the liver returned to normal. I think this stereo-photogrammetric method that has been elaborated in collaboration with Dr Hjelmström, Dr Ohlson and Dr Hagberg will be of value in measuring the volume of the liver under different conditions. It is simple and it is very exact.

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SUGGESTED AREAS FOR FUTURE CONFERENCE DISCUSSION AND FOR RESEARCH

Informal Group Interchange

Talbott I would like now to go from the beginning to end of the conference table and have any comments that anyone would like to make regarding this conference, suggestions of subject matter for future conferences, or suggestions regarding investigation. Jeff, do you want to start?

Crismon I think one of the problems likely to be fruitful is an examination of the area available for exchange of fluid in the capillary bed. A great deal of attention has been paid to changes of permeability as they are judged from the appearance of protein molecules in edema fluid, and to the flow of minute volumes of blood. It occurs to me that perhaps some of the phenomena, such as the one described by Dr Adams-Ray namely the reduction of edema in certain circumstances that were associated with relief of vasospasm, might possibly be related to an improvement of communication between perivascular spaces and the blood stream as a result of exposure of more capillary area. Perhaps similar considerations of area have to do with the rate of loss of fluid. It is not proper I think, to consider all capillaries open at the same time or to consider that a given flow rate is always associated with the same route from arterioles to venules. The more we learn about the exchange surface, the more we will understand about the relationship of the circulation to the injury produced by cold and to the recovery processes that are concerned with reversibility of cold injury

Talbott I would like to ask Dr Adams-Ray in what part of the vascular system the pooling takes place if there is an arteriolar constriction and venous constriction and pooling of blood in the parenchyma of the lungs or in the liver

Adams Ray If the hepatic venules and veins constrict, you will have a pooling in the vascular bed of the liver and perhaps secondarily in the portal system. In the lung Sjöstrand (58) has demonstrated that there are sinusoids that have a great capacity of

enlargement and constriction and that is the place where the pooling might take place.

Burch I would like to suggest that maybe in one of our sessions, we might discuss the sort of experiment that Dr Hegnauer described today cooling of the whole animal. This is an interesting subject.

Hegnauer Can we amplify that to include not only the so-called homotherm but also the hibernating animal?

Burch Yes.

Hegnauer It is a comparative problem, really hibernation versus artificial hibernation.

Burch It is difficult for me to suggest the course to take in the study of cold injury I think we need more people who are genuinely interested in cold injuries to work on the subject. It is my impression from these sessions that there really isn't a great deal being done on the subject. The field needs support because it obviously is an important problem, especially when we realize the military possibilities and the fact that a large part of the uninhabited areas of the earth are in the polar regions and probably a great deal of the natural resources will eventually have to be brought out of the cold areas.

It is my opinion that cold injury is a diffuse injury it is not localized in any one tissue It is vascular nerve osseous, and so forth. The responses and the manifestations we observe in our experimental animals and in man are determined by the degree of cooling, the duration of cooling, the rate of cooling and rewarming as well as the result of damaged tissues and their relative roles in repair Many phenomena are evident because of disturbances in functions of tissue necessary for repair Although freezing of blood vessels *per se* may have little to do with the damage to other adjacent tissues by freezing, the damaged vessels change the circulation and impair repair therefore they influence the sequelae noted. It appears that the lymphatic system has been neglected, particularly when swelling and edema are being considered. I have the impression that spasm of the lymphatics and problems of lymph drainage are important factors which come into play much as Dr Adams-Ray has pointed out for venous circulation.

Brinkhous A question still exists regarding the relation of the overall coagulability of the blood to cold injury It seems to me that an attempt should be made to study in an isolated manner the element of vascular occlusion in cold injury and to determine its role, if any in the production of necrosis. If this could be done

animal which is suitable for anticoagulant studies from the standpoint of their relationship with the problem in man?

Brinkhous As you know there are many of these clotting factors. More are being described every year One of the continuing studies in our laboratory is a species comparison of various coagulant factors. Because no two species are alike, certain criticisms can be made of the transfer of conclusions from one species to another I believe the dog, and perhaps the rat, are as suitable as any animal for studies of this type.

Meryman There is one subject, concerning which, as many of you know I have been carrying on rather a solitary crusade. That is the need, in local cold injury for a firm and constant differentiation between the freezing and the nonfreezing injury When we freeze tissue under well-controlled and measured conditions, dry it from the frozen state and imbed it, we can see the spaces which were occupied by ice crystals. It is perfectly evident that freezing at the rate which one would expect in a clinical case is going to cause a great deal of damage in tissue This damage will be principally plasmolysis, and the plasmolysis will be very severe One can t see whether or not there is membrane rupture, but there is certainly a serious derangement of the anatomy of the cells. On thawing, there is a reconstitution of the water so that the tissue often regains a more or less normal looking appearance as you see it under the microscope

In the studies that have been carried on with transillumination, one sees on thawing, a period of hyperemia followed by stasis. I don t feel that it is entirely justifiable to interpret that as being a purely circulatory response, because if there has been local subtle damage to each individual cell, without a massive derangement of overall structure, one will not see any specific evidence of injury to the cell. The dead cell, immediately after death, looks no different from the living cell. The only effect on tissue that will be seen will be in function, and the only function which can be seen at the time is that of the circulating blood so that the observation of massive circulatory damage does not necessarily mean that the damage has been circulatory in nature. It merely means that there has been a great deal of damage From my experience, I would say that freezing is a generalized damage throughout the tissue which will affect most cells It will be proportional to the hydration of the cell, which means, incidentally that skin will come off best in the case of freezing

Nonfreezing injury is a completely different type of trauma. It is

the result of an abnormal physiological situation, the result of vasoconstriction of one type or another change in viscosity of the blood, reduction in the oxygen capacity of the blood, and the net result, I think, is an anoxia to the tissue. If there is inadequate oxygen in the circulating blood, one would expect that tissue would suffer in the order of its anatomical location and its oxygen needs. That means that nerve tissue will suffer more on both counts, and in nonfreezing injury such as immersion foot, it is nerve tissue that suffers initially If over a period of time anoxia continues, there is increased damage to the nerve. Ultimately the anoxia will be sufficient to affect other tissues also, principally muscle and, ultimately sufficient tissue in general to cause necrosis.

The necrosis of nonfreezing injury I think is on a completely different basis than the necrosis of frostbite which is a freezing injury Clinically there is a very marked difference in the two. In immersion foot, there is a spectrum of injury down the foot, with the least injury proximally and becoming progressively worse toward the end of the extremity In frostbite, there can be virtually no significant injury right up to the line of demarcation and then there is gangrene. As I visualize this, the man with frostbite is exposed for a short period of time to cold anoxia, and to the effects of that brief anoxia. In first-degree frostbite, areas proximal to injury are identical in every way to a very mild immersion foot, as far as the sequelae go. However because the temperature is very low the progressive effects of anoxia do not continue for a long period of time and there is freezing and gangrene.

The important thing that one must bear in mind constantly is that these are two separate types of trauma, and if you are to produce a freezing injury experimentally you must recognize it as a freezing injury and not attempt to interpret the results in terms of a physiological situation such as the nonfreezing injury Clinically the freezing injury will be superimposed on a nonfreezing cold injury but to recognize the difference between these two types of injury is I think, extremely important.

The evidence for anoxia as the cause of damage is fair I refer here to some work by Kramer (2) in Germany in which he measured the oxygen saturation in a finger which was exposed to cold. He used spectrum analysis of transilluminated light to give the values of the saturation. Unfortunately it is in terms of skin temperature, so we can only suppose what the internal temperature might have been. But from 0 C. to 8 C., he finds oxygenation of 100 per cent. That would be interpreted as meaning that the tissue



FIGURE 40. Section of normal anterior tibial muscle. H. & E. x 150.



URE 41. Degenerative changes in muscle 2 hours after exposure. H. & E. 120

TABLE XLII

Redistribution of Potassium in Plasma and Edema Fluid
After Freezing at —35 C. to —37 C. for 4 Minutes

POTASSIUM IN PLASMA mEq./LITER

Hours After Exposure	0	6	12	24	48
Number of Readings	10	9	9	15	18
Mean Value	3.809	5.711	4.653	4.711	4.731
S. E.	±0.21	±0.23	±0.23	±0.24	±0.31
S. D.	±0.67	±0.68	±0.70	±0.94	±1.33
P	—	<0.01	0.01-0.02	<0.01	~0.02
Significant Difference From 0 Value	—	Yes	Yes	Yes	Yes

POTASSIUM IN EDEMA FLUID mEq./LITER

Hours After Exposure	0 (Plasma)	6	12	24	48
Number of Readings	10	10	12	18	12
Mean Value	3.809	4.305	4.744	4.578	5.270
S. E.	±0.21	±0.28	±0.18	±0.14	±0.21
S. D.	±0.67	±0.87	±0.63	±0.60	±0.73
P	—	~0.2	<0.01	0.02-0.05	<0.01
Significant Difference From 0 Value	—	No	Yes	Yes	Yes

Reprinted, by permission, from Pirozynski, W. J. and Webster, D. R.: Redistribution of potassium and sodium in experimental frostbite. *Surgical Forum*, Trans. Proc. 38th Am. College of Surgeons, Philadelphia, Saunders, 1953 (pp. 665-70)

There does seem to be a gradient in tissues. In our experience the gradation is nerve, muscle, skin and large blood vessels. There is a progressive degeneration resulting in final destruction of the axonic elements as shown in Figures 37, 38, and 39 (pp. 197-199). Since small fibers represent the nerve supply to the blood vessels and control the vasomotor functions, circulatory stasis following severe cold injury might be the result of this degenerative process.

In other experiments while exposing rabbits' legs to severe cold, the skin was not destroyed but the muscles suffered severe damage. Figures 40, 41, and 42 show the progressive disintegration of muscle cells and inflammatory reaction which occurred. Later stages show that this injury is repaired by fibrous tissue so there is irrevocable damage as far as the individual muscle cells are concerned (3).

We did some electrolyte studies of the muscle which corresponded to these muscle specimens. The redistribution of potassium and sodium in plasma, edema fluid and muscle tissue following exposure of one rabbit's leg to −35° C. to −37° C. has been investigated (4,5). Progressive loss of potassium from the injured muscle tissue due to rapid breakdown of the cells occurred (Table XLI). The release of potassium resulted in hyperpotassemia and accumulation of it in the extracellular fluid (Table XLII, Figure 43). There

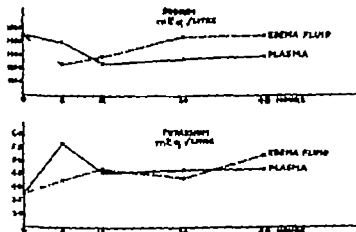


Figure 43. Graphic presentation of changes in sodium and potassium in plasma and edema fluid after freezing at −35 C to −37 C for 4 minutes. Reprinted, by permission, from Pirozynski, W. J. and Webster, D. R. Redistribution of potassium and sodium in experimental frostbite. *Surgical Forum*. Trans. Proc. 38th Ann. College of Surgeons. Philadelphia, Saunders, 1953 (pp. 665-70).

Medicine not only VD control officers but Cold Injury control officers. That is purely from the practical side.

From the point of view of further research in the field of cold injury I think that the field is wide open and what we need to know is how to stimulate young people to work in it. I would like to know something about the metabolic requirements and metabolic efficiency of human peripheral tissues studied in, let's say a Warburg apparatus or with Cartesian divers, with regard to different rates and degrees of cooling and freezing and different rates and degrees of warming up. As far as I know there has been no concerted effort to tackle this field at all.

The other thing which interests me, not so much in regard to cold injury but in regard to living in the cold, is the endocrinological changes which occur with exposure to cold, or to living in a cold climate. I think the time has come to measure blood levels of various hormones like TSH ACTH and thyroxin in people exposed to the cold and becoming acclimatized if there is such a thing as acclimatization.

Hegnauer In that same connection, we have planned to measure the peripheral circulation, the circulation through the femoral artery in dogs immersed in an ice bath. The hind leg, even the deep musculature close to the femur drops down to a temperature of about 10 C or 12 C. after an hour and a half or two hours in the bath, and although I have not measured the subcutaneous temperature in the paw for instance, I think we probably have every reason to suppose that that is very much colder and much closer to the bath temperature.

From the overall oxygen consumption of the animal, which has been measured, one can say that at a heart temperature of about 17 C the overall oxygen consumption is only about 14.5 or 15 per cent of the normal.

Talbott What was the temperature, again?

Hegnauer It is a heart temperature of 17 C. which means that out farther in the periphery for instance in the paws and even in the cold muscles the oxygen consumption must be very very low. I don't know at what temperature the oxygen consumption is going to approach zero If you look at the curve of diminishing oxygen consumption with a fall in temperature, it looks as though it might approach zero somewhere around 10 C. or 12 C., but that is for the animal as a whole. As far as immersion foot is concerned, supposing there is still a measurable oxygen consumption of these peripheral tissues when the limb is immersed in an 8 C. or 10 C.

bath for a prolonged period of time, it seems conceivable that the constriction which occurs might be maximal, blocking all blood flow thereby starving those tissues which at that temperature still have a slight but measurable oxygen consumption, and producing damage by anoxia.

Meryman Of course, your figure of the oxygen consumption of the animal at 17 C. is not necessarily the amount of oxygen that the tissue would like to consume. It may be merely the amount that it is able to consume, with a restricted circulation peripherally

Hegnauer It represents the demand If you feed the animal 100 per cent oxygen, and artificially respire him, his oxygen consumption does not increase. It makes no difference whether you respire him with air or oxygen.

Talbott There is one other bit of evidence I assume which would be the fact that there is no demonstrable damage later

Hegnauer There is no demonstrable damage later for the reason that you can warm the dogs from those temperatures You can t hold them at those temperatures, but if you put them in a hot bath immediately and rewarm them, if they were not too heavily anesthetized beforehand for instance, if one uses ether as pre-immersion anesthesia instead of pentothal or nembutal, they wake up at about 27° C. or 28° C. and may struggle to get on their feet As soon as the tenseness from shivering is eliminated, they can get on their feet. They will eat and work without evidence of lameness or pain.

As far as you can observe there is absolutely nothing the matter with them. I might add that the total cooling period is only from two to three hours, not enough to reveal anything with respect to possible hypoxia in the extremities such as Dr Meryman s question suggests

Kark Do they get cyanosis?

Hegnauer No there is no cyanosis

Adams-Ray Do you think in nonfreezing cold injury it is anoxia that kills tissue?

Meryman I believe so

Adams-Ray But you tell us and we know from clinical work, that if you have put a tourniquet on your leg and if you have that on for two hours —

Hegnauer But the body is at a warm temperature and the oxygen demand increases at a warm temperature.

Meryman Two hours is not an adequate time. Two hours in immersion will not give immersion foot. The tissue loss from immersion foot is a loss after exposure of days, perhaps a week or more.

Siple Therefore, you are dealing with a relative situation in respect to time.

Meryman You are dealing with death from cumulative anoxia.

Burch It is slow

Meryman That is why I say the differentiation between frostbite, a freezing injury which occurs in a short period of time, must be made from the nonfreezing injury which occurs as the result of an exposure of days.

Adams Ray You have nonfreezing cold injuries that occur in a very short time.

Meryman How short?

Adams Ray Half an hour or an hour exposure. In that cold spell in 1940, we had nonfreezing injuries The chaps coming out of the restaurants, at night, had no fur caps. They had an exposure time of about 10 or 15 minutes, and they had cold injury

Meryman How do you know it was a nonfreezing injury?

Adams Ray Some of the patients themselves had not observed any stiffness in their ears. I saw all patients who came to the hospital during the night, and their ears were not frozen stiff.

Meryman Well, I would want a little more evidence that there was not some ice crystal formation in the more hydrated tissues, or that the men had not thawed the ear out by the application of a hand prior to coming in, or some such thing.

Blair The miraculous thing is how rapidly a freezing injury can thaw under certain conditions I am highly skeptical of many of the so-called very low temperature frostbites about which it is stated that there was no ice formation and no freezing, because I have personally observed a man with a very severely frozen face which completely thawed in a few minutes at room temperature. I think a man can come into a hospital or clinic with a frozen part, walk the length of the hall, and actually be completely thawed by the time he gets to a doctor You can t say he did not have ice formation or a freezing injury unless you see him out in the cold before he has been rewarmed. The same thing is true of a soldier He can walk from a foxhole back to the battalion aid station, and though he has not been rewarmed, the activity of walking and exercise will thaw the injury before he ever reaches a warm environment.

Adams-Ray I saw some patients in the mountains, actually whose feet and hands were numb and they were in an ischemic stage. There was absolutely no freezing. That is what I saw in two cases, and that is nothing. However we do have nonfreezing cold injury without long exposure.

Meryman What were the sequelae of these injuries, gangrene?

Adams Ray Edema. Pain.

Meryman That is an extremely mild injury and you would call the case frostbite only because it occurred in dry cold. It would not necessarily have to be a freezing injury I believe that a freezing injury except possibly a very quick freezing of the skin, will inevitably result in tissue loss.

Hegnauer I would like to differentiate the two types of injury One is a temperature injury as such, and the other is an actual ice crystal formation injury

Meryman Precisely

Shumacker The same thing bothers me which I am sure bothers all of you. I certainly think we have to differentiate cold injuries, such as trench foot and immersion foot which occur from prolonged exposure to mild wet cold, from those which occur relatively quickly from exposure to intense and more or less dry cold. It seems to me that the evidence is not at hand to support the assumption that all injuries resulting from brief exposure to relatively dry intense cold are associated with actual ice crystal formation. Such an assumption, I feel, is based upon an awfully flimsy basis.

Blair That there is no ice formation is on a very flimsy basis also. Why can you cool a man down in the cold room to a skin temperature below 0 C and see no sign of freezing injury at all? I am sure that Dr Horvath has done that. I have done it many times and have kept men near zero

Horvath And minus zero.

Blair No cold injury whatsoever occurs My explanation of why it doesn't occur is that there is no ice crystal formation or actual freezing of the tissue. I have seen men held for four and six hours at a skin temperature near 0 C., with no pathology whatsoever resulting from it.

Meryman But if you held him there for days, then you would have something equivalent to immersion foot or trench foot.

Horvath: I don t think you have to hold him at zero for that long.

Meryman No no but the time period involved for a nonfreezing injury is of a considerably different order of magnitude than for the freezing injury

Horvath: We just finished studying four people who were living in the nude at approximately 60 F lying quietly with no movement whatsoever except to go to the toilet for five minutes once a day for about a week. I might say that of those four there were

tissues. Then, in association with plasma volumes, we did the sulfacyanate space, and found that the sulfacyanate space decreased by about 20 to 25 per cent.

Webster How are your electrolytes?

Hegnauer We haven t done electrolytes but in none of the work is there any indication of stagnation of the blood in pockets, except for the plasma. It looks as though plasma skimming occurred, that is, some vessels were constricted down to the point where they permitted some plasma to leak in there but permitted no cells to get in, and the cells would bypass those passages. That is only a suggestion, however

Burch I might indicate that we have data to show that chloride is found in cells in relatively large amounts in normal and abnormal man.

Hegnauer The chloride space is actually decreasing, not increasing, and the sulfacyanate space is decreasing. The chloride space decrease, according to our first measurement, I think, can be accounted for by the fact that at 28 C., where this shift of water from the chloride space, the extracellular compartment, is maximum, shivering is at a maximum, so that you are increasing the cellular osmotic pressure and drawing in water at the expense of the chloride space rather than the plasma.

Burch Of course, the first time, you may be measuring intra- and extracellular chloride space, and the second time only extracellular chloride space.

Hegnauer Do your measurements indicate that the cells take up chloride normally?

Burch Oh, yes, that s right, and a large amount, too. Of course, our studies were with radioactive chloride, Cl^{36} We have shown chloride to go in and out, especially in large amounts in heart failure. Robert Pitts reported at the fall meeting of the American Physiological Society in New Orleans that he could cause about 20 per cent of extracellular chloride to enter cells by intravenous injection of concentrated solutions of sodium bicarbonate in dogs. Our studies, over the last five or six years, have indicated even larger shifts for chloride and even large ones for sodium.

Hegnauer The bicarbonate concentration of the dog does not increase very much in response to hypothermia, so I don't know

Horvath It appears to me, from listening to what people have suggested as possible future things, that there are at least two major problems that we might look into. One is the relative demands by and requirements of various tissues under different thermal injury

or different thermal stresses, over a long period especially in terms of the cold. This relates almost immediately to a better understanding of the relative role of anoxia and the effect of cold, not only at a body temperature of 37° C. but at variable temperatures down to 15° C. on the oxygen association curve and the way in which cold influences the liberation and the uptake of oxygen in various parts of the body. It certainly is very obvious from all that has been said that although the temperature of the body may be 36° C., a slight hypothermia, there may be portions of the body which will be at 20° C., 15° C., 10° C. or even less. All these various temperature gradients in the body would certainly markedly modify the total end picture of dissociation of oxygen from hemoglobin, therefore another thing to look into would be the effects in one tissue and then the effects on the total tissues.

Another problem that we have been bypassing all along is the so-called defensive reactions of the body against cold injury. That certainly should be corrected. For instance, I think several times somebody mentioned the fact that shivering is a very nice defense reaction, that it might protect the individual against cold injury quite efficiently. I don't believe that anyone here can actually say that shivering, because we really cannot grade it in a very accurate way, gives you a total caloric excess of so much. In fact, I don't think we actually know the real stimulus to shivering.

Back in 1932, I believe it was Swift (6,7) who said that the depression of skin temperature or the chest, I believe it was, to 19° C. was a shivering stimulus and Bazett has said that there are temperature receptors slightly underneath the skin. Blood temperatures have been indicated as stimuli for shivering. Actually we don't know.

There are other defensive reactions which we probably have not considered. For instance let us assume that maybe some of the people, who said that there is a hydration of the cells were right, but there isn't enough information to say whether or not there is such a change. The question then arises, is the hydrated cell a better protected cell against the cold than one that is not hydrated? Does an individual who has been excessively hydrated receive more severe and rapid cold injury or is he less susceptible to cold injury? There are other defense reactions which we have not even considered as yet and certainly they can be valuated from the standpoint of their effect upon protection against cold injury and, further more maybe as the means of prophylaxis against the terminal effects

agents diminished somewhat the extent of gangrene. As I recall them your results were not dramatic but definite.

Webster Yes, that's right.

Shumacker During the last year I have talked with a number of individuals about the question of sympathetic denervation in human beings with frostbite and have analyzed my own experiences (9) Dr de Takats tells me that he has seen a number of patients in Chicago and at the Great Lakes Naval Hospital with apparent equal injury of both feet in whom an early unilateral sympathectomy was carried out. I recognize the difficulty in estimating bilateral involvement as equal in degree. Nevertheless, in these patients the line of demarcation between viable and nonviable tissues developed much more rapidly in the denervated extremity and definitive treatment could be carried out much earlier on that side so that often this extremity would be healed long before the other Although he could not be sure that the sympathectomy resulted in actual saving of threatened tissue, he feels that the procedure altered favorably the course of events and permitted much quicker healing. Last week at Camp Atterbury I saw an officer whom Colonel Orr and I had met in Korea about a year ago He told me that, shortly after we saw him in Korea, he was given another assignment which placed him in immediate proximity to a ROK medical unit. Because the ROKs were badly handicapped with regard to other possible therapeutic aids, they were anxious to try the effect of sympathectomy on patients with frostbite and asked him to teach them the technique of lumbar sympathectomy They performed unilateral sympathectomies upon the next 50 patients whom they encountered. This officer had the impression, as did the ROK officers, that the operation brought about a dramatic and favorable alteration in the course of events, with rapid disappearance of pain and edema, quicker demarcation and more rapid healing. Following this experience they apparently felt justified in performing early bilateral sympathectomy upon approximately 150 patients. It was generally felt that there was a very pronounced shortening of the period of disability and a much earlier return to full duty

I do not mention these observations as a proposal that all cases be treated by sympathetic denervation. Unfortunately this experience will be essentially lost as it is not likely to be reported in the literature. I know of it only from hearsay but my informant, who is a bright and observing person, felt that there was no question about the generally favorable influence resulting from this treatment.

During the past winter we had one very interesting patient in

Indianapolis a man who according to my best judgment was destined to lose at least his great toe and in whom the eventual loss was only a tiny area of superficial necrosis of skin. During the phase of reactive hyperemia when the entire foot was quite warm, the great toe remained cyanotic and cold. Furthermore, there were large vesicles proximally and none on his toe. We have learned that such signs are indicative of impending deep gangrene of the entire toe. After early sympathectomy the color and warmth of the toe improved and only a small superficial ulcer resulted which healed rapidly

Obviously one such patient means little, but if over a period of time, one should encounter a number of similar cases, it would certainly contribute a great deal to one s understanding of the possible aid of sympathetic blockade in the early treatment of frostbite. If we take advantage of every opportunity to make careful observations perhaps eventually the cumulative experience will be sufficient to make the best management of cold injuries a great deal clearer I feel optimistic that progress will continue and that with enough people working in the field it may be possible to bring about a better understanding of the fundamental processes concerned in cold injuries as well as a better insight into effective measures for their prevention and treatment.

Siple I have been very much impressed by the remarks in the last hour here, because I have seen, I feel, an advance or a clarification in theory to the point that I would almost go so far as to predict that in our third conference we will be able to separate the two major aspects of cold injury which have confused us particularly last year and to some extent this year I feel that the comments Dr Webster made with respect to the electrolytes are a clue to the probable fact that we do have a fractionation of the colloids in slow freezing which is a real cause of death of the tissue. In quick freezing there isn t time for fractionation, and therefore the molecular particles are in juxtaposition and are capable of viability when they are thawed out again.

G W Scarth (10) and his colleagues have been studying plant tissues in respect to frost resistant plants and the tender plants that are killed with just a slight touch of frost. They have made the cell studies in great detail and have given an indication of the kind of deterioration that is apparently within the cell structures themselves.

I was also very much encouraged by the remarks that Dr Hegnauer made with respect to anoxia for I feel that in deaths due to cold exposure and often erroneously attributed to freezing.

there is a form of anoxia related to the variable metabolic demands of tissues at different temperatures.

I have been particularly concerned with this subject because I lost a friend during the past year by death from cold exposure at a temperature of −30 F He was a medical man himself, carrying on experimentation. The autopsy that was made showed no clear cut evidence of what actually caused his death. However perhaps the most abnormal situation reported was congestion in his lungs which would indicate that he died from a respiratory cause. He was aware and I believe concurred in the theory discussed after our last Cold Injury Conference that overnight deaths due to cold exposure are caused by a progressive anoxia. The deeper core tissues still demand a high metabolic oxygen rate, but the peripheral tissues demand less, and apparently the latter exercise major control over the respiration and the blood circulation. Therefore, relatively speaking, anoxia begins to affect the tissues with a high oxygen demand, such as the viscera for example, even though there is adequate oxygen for the peripheral and obviously cold tissues. Perhaps the first critical areas to be affected by anoxia are the higher motor centers of the brain and as a further consequence the whole organism dies. I believe my friend, Dr Dana Coman, slept to death in a temperature of −30 F He was doing a follow-up experiment on two men who had carried out a similar experiment the night before. The two men dressed in special clothing had gone to sleep lying on top of their sleeping bags. They woke up after an hour and a half because of violent shivering and got into their sleeping bags, warmed up and survived the night very well. Dr Coman did not wake up from the initial phase of the experiment. There was perhaps, not a full recognition of the dangers involved on his part and not enough controls around to watch him.

However it does lead me to believe at least that the anoxia aspects of cold exposure are extremely important and should perhaps be examined in order to explain these deaths by exposure overnight which stand in such sharp contrast to the survival by individuals exposed under worse conditions frequently wearing less clothing, and exposed for three or four days I am not sure that Dr Horvath agrees with me completely but I feel that shivering seems to play an important part. If a person exposed to cold shivers, I don't believe he will be in danger of death, however if he does not shiver he is in grave danger of sleeping to death in the cold. The failure of the shivering mechanism may be due to many factors, such as a lack of stimulus of a sharp thermal gradient through

50 patients with frostbite and some 74 controls. Our data do not show any clear cut distinction between the two groups however, the cold injury patients tend to be immature, passive individuals with suggestive traits of a schizoid personality From the data of the psychiatric study one of our investigators proposed the idea of a personality inventory for the purpose of screening men for cold weather operations in other words, a measure for predicting which man might be most apt to incur frostbite. This type of inventory utilizes 20 items from the Minnesota Multiphasic Inventory Test on which the answers given by the frostbite patients were distinct from the responses obtained from the controls. This is a type of approach for screening of troops that is very provocative, because this method has not been field-tested and it is still in the questionable stage at the present time.

Our nutritional survey in the winter of 1952 revealed that many of the frostbite patients had not received what we considered an adequate amount of food. Their caloric intake just preceding injury was as low as from 1500 to 1800 calories. The serum ascorbic acid surveys showed the frostbite patients not to be markedly different from various control groups. Ascorbic acid surveys were conducted on some 2400 combat soldiers. Further work is needed in the nutritional field.

Schuman I should like to say that as an epidemiologist, I am quite impressed with the similarity between the epidemiology of trauma, such as cold injury and the epidemiology of both the acute infectious diseases and the chronic diseases.

I feel that much can be gained in future study of the epidemiology of the particular host and agent relationship in trauma, especially the modifying factors. With this particular concept in mind, I believe that neither an epidemiologist nor the laboratory physiologist can claim the preference of approach to this particular problem. I believe that because this entity is a multiple factor phenomenon progress in the prevention of this particular trauma will be the result of a combination of exploration in all the fields which we have heard discussed here in the last two days. I say this particularly because I am impressed with the evidence of individual variations in susceptibility even though we have not proposed or presented any distinct proof that such exists.

I presented to you differences in the risk of attack between the races. I did not necessarily prove or claim a difference in susceptibility but only showed that a difference between the races did exist. I am going to be surprised in the future if such a difference

is proved to be on grounds other than susceptibility I say this because in certain chronic and acute infectious diseases, we find racial differences in susceptibility and in others, no racial differences in susceptibility At the moment, we do not know whether or not differences in true susceptibility play a role in cold injury as far as racial differences are concerned. I think, therefore, that coupled with field investigations in epidemiology one must continue the hunt for these subtle differences between the races and between individuals as far as tissue susceptibility is concerned.

I am one of those diehards who is neither amazed nor dismayed by the failure of our pre-exposure studies and who still proposes that in the future, especially under military operations, a more elaborate and extensive pre-exposure study be undertaken, with special attention to the field of vasomotor stability Furthermore, I feel that the neuropsychiatric study which Colonel Orr has mentioned must be expanded, because I personally believe that in this particular endeavor there lies promise for progress in understanding individual differences, which may be the bases for such variations in susceptibility

Colonel Orr has mentioned that the afflicted individuals tend to be immature schizoid and, passive and frequently are called by the psychiatrist the passive-aggressive individuals, a term which is not really contradictory but means that the individual is passive in his reaction to stress but mentally is aggressive in what he does about that stress. We have some field evidence to back up this particular tendency or this concept of a tendency comparison of our controls to the patients showed that the in ide situations, whether they were pinned ol, w they were in a vehicle, whether th e nnal patrol or on a combat patrol did mu re th the patients (Table XI

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6. SWIFT R. W The effects of low environmental temperature upon metabolism technic and respiratory quotient. *J Nutrition* 5, 213 (1932)

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8 SHUMACKER, H. B., JR., and LEMPKE, R. E. Recent advances in frostbite, with particular reference to experimental studies concerning functional pathology and treatment. *Surgery* 30, 873 (1951)

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APPENDIX AUTOBIOGRAPHICAL SKETCHES OF PARTICIPANTS

ALAN C. BURTON: I am in the Department of Biophysics. It may be quite unnecessary but I find it useful to explain what I mean by a biophysicist, he is just a particular kind of physiologist who when he sees physiological events and watches the behavior of living things, is interested in the physics that lies behind that behavior just as the biochemist is interested in the chemistry My interest in the physiological effects of cold really dates from my turning from physics to physiology and working on human calorimetry and the heat exchanges of the animal and the human body Then I had the privilege of going to learn, study and do some research with Dr Bazett, who has influenced so many of us here, and there I continued my interest in the temperature regulation of the body From that study I was led into an investigation of the control of the peripheral circulation in accordance with the demands of the temperature regulation. During the war I was put on practical problems of men faced with unusual environments, such as cold and altitude. I hope some day to do some more work on the effects of cold, but at the moment I have been concentrating on the peripheral circulation.

JEFFERSON M. CRISMON My first interest in cold began with some work on hypothermia done under the sponsorship of the Markle Foundation some years ago. Like Dr Burton, during the war we worked on some practical problems but these were investigated at a slightly more fundamental level, and our work concerning frostbite was done not on men but on animals. Since that time, because of the dearth of detailed information about gangrene in its relation to ischemia, we have studied the metabolic changes in peripheral tissues that have been rendered ischemic in one way or another My associate Dr Frederick A. Fuhrman, has gone on with that aspect of the work to a considerable degree· I have become more interested in the capillary circulation.

GEORGE E. BURCH I have been interested in the peripheral blood vessels. Using it primarily as a contrast environment, our

operations My interest in cold and cold injury extends over the past 25 years including four expeditions to the Antarctic as well as some trips into the Arctic. During World War II, I was sent on a mission to Europe to examine the causes of trench foot among our troops. In the winter of 1951-52 I visited Korea to study winter combat problems, including factors influencing cold injury I personally have had as much exposure to cold as anyone here. During my association with the Army in and out of uniform during the past ten years I have been concerned also with the research and development of clothing and foot gear as a preventive to cold injury particularly the concepts involving vapor-barriers

LEONARD M. SCHUMAN: As an epidemiologist, my interest in cold injury may be expressed as one of philosophy primarily because I hold the belief that epidemiological principles are just as applicable to chronic disease and trauma as they are to communicable disease. I never dreamed that the opportunity would arise to prove that belief to myself and possibly to others until the fall of 1951 when the Surgeon General of the Army asked me to make a trip to Korea. Recommissioned by the U S Public Health Service, I went with the team headed by Colonel Orr This trip gave me interesting insight into the application of epidemiological principles to cold injury

KENNETH D ORR: My first contact with cold injury was on the wards at Cook County Hospital, Chicago, Illinois, in January 1939. My second contact was made in Italy during the winter of 1944-45 I was a Regimental Surgeon in a unit which unfortunately had a high incidence of trench foot. It was at this time that I became interested in cold injury particularly in the preventive aspects In November 1950, while serving as Chief of the General Medical Section, Osaka Army Hospital, Osaka, Japan, I received the first frostbite cases that occurred among the American troops in Korea. A short time later I opened and was placed in charge of the Cold Injury Center for the Far Eastern Command. As the result of our work in this Center I was ordered to the United States in the summer of 1951 to prepare a report on cold injuries incurred in Korea. I was sent back to Korea the winter of 1951-52 with a team to

conduct field studies on cold injury At the present time we are engaged in the task of preparing the results of this study

JOSEPH R. BLAIR I am presently engaged in setting up a research project on experimental cold injury in the Department of Physiology at the Harvard Medical School under Dr Eugene Landis. My first contact with cold came as a physiologist, investigating temperature regulation at the University of Alabama with Dr Allen Koller Then my interest lay dormant until Colonel William S Stone advised me that I was going to Fort Churchill in Canada for the purpose of setting up a cold stress research laboratory I spent the next three winters at Fort Churchill and four years at the Army Medical Research Laboratory at Fort Knox, Kentucky studying acclimatization to cold and experimental cold injury During the past two winters I have had the good fortune of being associated with Colonel Orr and his clinical studies in Korea. I am at present particularly interested in the physiopathology of cold injury sequelae and plan to work with Dr Landis in Boston on that problem for the next two or three years.

HARRIS B. SHUMACKER: My special interests are in the cardiovascular field. Before World War II I had no particular interest in cold injuries. I became much more concerned with the general problem when, during the latter half of World War II, I directed one of the three Army Vascular Centers. Here my associates and I were responsible for the care of a great many individuals who had sustained vascular injuries. Because of that stimulating experience and because of the dearth of knowledge concerning cold injuries in general, I was prompted to undertake some animal experimentation and a fairly active investigative program has been going on in my laboratory since then. My interest also has been kept alive by my relationship with the Armed Forces as one of the consultants who helped organize the last cold injury study team and its program in the Far East, and as one of those who had the opportunity to observe the work of this team in Japan and Korea in 1951-52.

JACK ADAMS-RAY My first interest in cold injuries dates from a frost bite of my own when skiing in the mountains 20 years ago In 1940-41 we had a very cold winter and I tried

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JOSEPH R. BLAIR: I am presently engaged in setting up a research project on experimental cold injury in the Department of Physiology at the Harvard Medical School under Dr Eugene Landis. My first contact with cold came as a physiologist, investigating temperature regulation at the University of Alabama with Dr Allen Keller Then my interest lay dormant until Colonel William S. Stone advised me that I was going to Fort Churchill in Canada for the purpose of setting up a cold stress research laboratory I spent the next three winters at Fort Churchill and four years at the Army Medical Research Laboratory at Fort Knox, Kentucky studying acclimatization to cold and experimental cold injury During the past two winters I have had the good fortune of being associated with Colonel Orr and his clinical studies in Korea. I am at present particularly interested in the physiopathology of cold injury sequelae and plan to work with Dr Landis in Boston on that problem for the next two or three years.

HARRIS B. SHUMACKER: My special interests are in the cardiovascular field. Before World War II I had no particular interest in cold injuries. I became much more concerned with the general problem when, during the latter half of World War II I directed one of the three Army Vascular Centers. Here my associates and I were responsible for the care of a great many individuals who had sustained vascular injuries. Because of that stimulating experience and because of the dearth of knowledge concerning cold injuries in general I was prompted to undertake some animal experimentation and a fairly active investigative program has been going on in my laboratory since then. My interest also has been kept alive by my relationship with the Armed Forces as one of the consultants who helped organize the last cold injury study team and its program in the Far East, and as one of those who had the opportunity to observe the work of this team in Japan and Korea in 1951-52.

JACK ADAMS-RAY My first interest in cold injuries dates from a frost bite of my own when skiing in the mountains 20 years ago In 1940-41 e had a ery cold winter and I tried

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